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Preliminary Draft

Review of the National Ambient Air Quality Standards for Particulate Matter:

Policy Assessment of Scientific and Technical Information

OAQPS Staff Paper

Notice

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1. INTRODUCTION

1.1 PURPOSE

The purpose of this preliminary draft Staff Paper, prepared by the Office of Air Quality Planning and Standards (OAQPS), is to identify the key policy-relevant scientific information contained in the EPA draft document, *Air Quality Criteria for Particulate Matter – Second External Review Draft* (EPA, 2001; henceforth referred to as draft CD and cited as CD), recognizing that this information is still provisional at this time. Preliminary and planned staff analyses (e.g., analyses of air quality and visibility data, human health risk assessment) are also presented for public and peer review prior to completing and incorporating results of such analyses into a subsequent draft of this document.

When final, this Staff Paper will evaluate the policy implications of the key studies and scientific information contained in the final *Air Quality Criteria for Particulate Matter* (henceforth the CD), and identify the critical elements that EPA staff believe should be considered in the review of the national ambient air quality standards (NAAQS) for particulate matter (PM). This assessment is intended to help "bridge the gap" between the scientific review contained in the CD and the judgments required of the Administrator in setting NAAQS for PM (*Natural Resources Defense Council v. Administrator*, 902 F.2d 962, 967 (D.C. Cir. 1990)). Thus, emphasis will be placed on identifying those conclusions and uncertainties in the available scientific literature that the staff believes should be considered in selecting PM indicators, forms, averaging times, and levels for the primary (health-based) and secondary (welfare-based) standards, which must be considered collectively in evaluating the health and welfare protection afforded by PM standards. The final Staff Paper will present factors relevant to the evaluation of current primary and secondary NAAQS, as well as staff conclusions and recommendations of options for the Administrator to consider.

While this preliminary draft Staff Paper should be of use to all parties interested in the NAAQS review, it is written for those decision makers, scientists, and staff who have some familiarity with the technical discussions contained in the draft CD.

1   **1.2   BACKGROUND**

2   **1.2.1 Legislative Requirements**

3   Two sections of the Clean Air Act govern the establishment and revision of the NAAQS

4   (42 U.S.C. 7401 to 7671q, as amended). Section 108 (42 U.S.C. 7408) directs the Administrator

5   to identify pollutants that "may reasonably be anticipated to endanger public health and welfare"

6   and to issue air quality criteria for them. These air quality criteria are intended to "accurately

7   reflect the latest scientific knowledge useful in indicating the kind and extent of identifiable

8   effects on public health or welfare which may be expected from the presence of [a] pollutant in

9   ambient air . . . ."

10   Section 109 (42 U.S.C. 7409) directs the Administrator to propose and promulgate

11   "primary" and "secondary" NAAQS for pollutants identified under section 108. Section

12   109(b)(1) defines a primary standard as one "the attainment and maintenance of which in the

13   judgment of the Administrator, based on such criteria and allowing an adequate margin of safety,

14   are requisite to protect the public health."[1] A secondary standard, as defined in Section

15   109(b)(2), must "specify a level of air quality the attainment and maintenance of which, in the

16   judgment of the Administrator, based on such criteria, is requisite to protect the public welfare

17   from any known or anticipated adverse effects associated with the presence of [the] pollutant in

18   the ambient air." Welfare effects as defined in section 302(h) [42 U.S.C. 7602(h)] include, but

19   are not limited to, "effects on soils, water, crops, vegetation, man-made materials, animals,

20   wildlife, weather, visibility and climate, damage to and deterioration of property, and hazards to

21   transportation, as well as effects on economic values and on personal comfort and well-being."

22   Section 109(d)(1) of the Act requires that "not later than December 31, 1980, and at 5-

23   year intervals thereafter, the Administrator shall complete a thorough review of the criteria

24   published under section 108 and the national ambient air quality standards . . . and shall make

25   such revisions in such criteria and standards . . . as may be appropriate . . . ." Section 109(d)(2)

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[1]The legislative history of section 109 indicates that a primary standard is to be set at "the maximum permissible ambient air level . . . which will protect the health of any [sensitive] group of the population," and that for this purpose "reference should be made to a representative sample of persons comprising the sensitive group rather than to a single person in such a group" (S. Rep. No. 91-1196, 91st Cong., 2d Sess. 10 (1970)).

1   requires that an independent scientific review committee "shall complete a review of the criteria .

2   . . and the national primary and secondary ambient air quality standards . . . and shall recommend

3   to the Administrator any . . . revisions of existing criteria and standards as may be appropriate . . .

4   ." Since the early 1980's, this independent review function has been performed by the Clean Air

5   Scientific Advisory Committee (CASAC) of EPA's Science Advisory Board.

6   The U.S. Court of Appeals for the District of Columbia Circuit has held that the

7   requirement for an adequate margin of safety for primary standards was intended to address

8   uncertainties associated with inconclusive scientific and technical information available at the

9   time of standard setting. It was also intended to provide a reasonable degree of protection

10   against hazards that research has not yet identified (*Lead Industries Association v. EPA*, 647 F.2d

11   1130, 1154 (D.C. Cir 1980), <u>cert. denied</u>, 101 S. Ct. 621 (1980); *American Petroleum Institute v.*

12   *Costle*, 665 F.2d 1176, 1177 (D.C. Cir. 1981), <u>cert. denied</u>, 102 S.Ct. 1737 (1982)). Both kinds

13   of uncertainties are components of the risk associated with pollution at levels below those at

14   which human health effects can be said to occur with reasonable scientific certainty. Thus, by

15   selecting primary standards that provide an adequate margin of safety, the Administrator is

16   seeking not only to prevent pollution levels that have been demonstrated to be harmful but also

17   to prevent lower pollutant levels that may pose an unacceptable risk of harm, even if the risk is

18   not precisely identified as to nature or degree.

19   In selecting a margin of safety, the EPA considers such factors as the nature and severity

20   of the health effects involved, the size of the sensitive population(s) as risk, and the kind and

21   degree of the uncertainties that must be addressed. The selection of any particular approach to

22   providing an adequate margin of safety is a policy choice left specifically to the Administrator's

23   judgment *(Lead Industries Association v. EPA*, <u>supra</u>, 647 F.2d at 1161-62).

24

25   **1.2.2   History of PM NAAQS Reviews**

26   National ambient air quality standards for PM were first established in 1971, based on the

27   original criteria document (DHEW, 1969). Particulate matter is the generic term for a broad

28   class of chemically and physically diverse substances that exist as discrete particles (liquid

29   droplets or solids) over a wide range of sizes. Particles originate from a variety of anthropogenic

1   stationary and mobile sources as well as natural sources. Particles may be emitted directly or

2   formed in the atmosphere by transformations of gaseous emissions such as sulfur oxides,

3   nitrogen oxides, and volatile organic compounds. The chemical and physical properties of PM

4   vary greatly with time, region, meteorology, and source category, thus complicating the

5   assessment of health and welfare effects.

6   The reference method specified for determining attainment of the original standards was

7   the high-volume sampler, which collects PM up to a nominal size of 25 to 45 micrometers (μm)

8   (referred to as total suspended particles or TSP). The primary standards (measured by the

9   indicator TSP) were 260 μg/m^3, 24-hour average, not to be exceeded more than once per year,

10   and 75 μg/m^3, annual geometric mean. The secondary standard was 150 μg/m^3, 24-hour average,

11   not to be exceeded more than once per year.

12   In October 1979 (44 FR 56731), EPA announced the first periodic review of the criteria

13   and NAAQS for PM, and significant revisions to the original standards were promulgated in

14   1987 (52 FR 24854, July 1, 1987). In that decision, EPA changed the indicator for particles from

15   TSP to PM_{10}, the latter referring to particles with a mean aerodynamic diameter[2] less than or

16   equal to 10 μm. EPA also revised the level and form of the primary standards by: (1) replacing

17   the 24-hour TSP standard with a 24-hour PM_{10} standard of 150 μg/m^3 with no more than one

18   expected exceedance per year; and (2) replacing the annual TSP standard with a PM_{10} standard of

19   50 μg/m^3, annual arithmetic mean. The secondary standard was revised by replacing it with 24-

20   hour and annual standards identical in all respects to the primary standards. The revisions also

21   included a new reference method for the measurement of PM_{10} in the ambient air and rules for

22   determining attainment of the new standards. On judicial review, the revised standards were

23   upheld in all respects *(Natural Resources Defense Council v. Administrator*, 902 F. 2d 962 (D.C.

24   Cir. 1990), cert. denied, 111 S. Ct. 952 (1991)).

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[2]The more precise term is 50 percent cut point or 50 percent diameter (D_{50}). This is the aerodynamic
particle diameter for which the efficiency of particle collection is 50 percent. Larger particles are not excluded
altogether, but are collected with substantially decreasing efficiency and smaller particles are collected with
increasing (up to 100 percent) efficiency.

1   In December 1994, EPA presented its plan for the second periodic review of the criteria

2   and NAAQS for PM to the CASAC, and significant revisions to the NAAQS were promulgated

3   in 1997 (62 FR 38652, July 18, 1997). In that decision, the PM NAAQS were revised in several

4   respects. While it was determined that the PM NAAQS should continue to focus on particles

5   less than or equal to 10 μm in diameter, it was also determined that the fine and coarse fractions

6   of PM_{10} should be considered separately. New standards were added, using $PM_{2.5}$, referring to

7   particles with a mean aerodynamic diameter less than or equal to 2.5 μm, as the indicator for fine

8   particles, with PM_{10} standards retained for the purpose of regulating coarse-fraction particles.

9   Two new $PM_{2.5}$ standards were set: an annual standard of 15 μg/m^3, based on the 3-year average

10   of annual arithmetic mean $PM_{2.5}$ concentrations from single or multiple community-oriented

11   monitors; and a 24-hour standard of 65 μg/m^3, based on the 3-year average of the 98th percentile

12   of 24-hour $PM_{2.5}$ concentrations at each population-oriented monitor within an area. To continue

13   to address coarse-fraction particles, the annual PM_{10} standard was retained, while the 24-hour

14   PM_{10} standard was revised to be based on the 99th percentile of 24-hour PM_{10} concentrations at

15   each monitor in an area. The secondary standards were revised by making them identical in all

16   respects to the primary standards.

17   In May 1998, in response to challenges filed by industry and others, a three-judge panel

18   of the U.S. Court of Appeals for the District of Columbia Circuit issued a split opinion regarding

19   the NAAQS for PM. The Panel recognized the scientific basis for the PM NAAQS revisions,

20   stating that "the growing empirical evidence demonstrating a relationship between fine particle

21   pollution and adverse health effects amply justifies establishment of new fine particle standards."

22   Further, the Panel found "ample support" for EPA's decision to regulate coarse particle pollution,

23   although it vacated the revised coarse particle standards on the basis of PM_{10} being a "poorly

24   matched indicator for coarse particulate pollution" because PM_{10} includes fine particles.[3] More

25   generally, the Panel held (with one dissenting opinion) that the Clean Air Act, as applied and

26   absent further clarification, is unconstitutional because it "effects an unconstitutional delegation

27   of legislative power." Although the Panel stated that "the factors EPA uses in determining the

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[3] The 1987 PM_{10} standards remain in effect.

1   degree of public health concern associated with different levels of ozone and PM are reasonable,"

2   it remanded the NAAQS to the EPA, stating that when EPA considers these factors for potential

3   non-threshold pollutants "what EPA lacks is any determinate criterion for drawing lines" to

4   determine where the standards should be set. Also, consistent with EPA's long-standing

5   interpretation, the Panel unanimously held that in setting NAAQS EPA is "not permitted to

6   consider the cost of implementing those standards."

7   These two general rulings were appealed to the U.S. Supreme Court, and in February

8   2001, the Supreme Court issued a unanimous decision that reversed the Court of Appeals' ruling

9   on the constitutional issue and upheld its ruling on the cost issue. In so doing, the Supreme

10   Court upheld EPA's position on both issues. Because the Court of Appeals had not rendered

11   decisions on all issues related to the 1997 PM NAAQS that had originally been before that court,

12   the case was sent back for resolution of any remaining issues. The Court of Appeals has

13   scheduled further briefing on those issues this summer and fall. Although the litigation has not

14   yet been fully resolved, the $PM_{2.5}$ standards have not been revoked and thus remain in place.

15   On October 23, 1997, EPA published its plans for the current periodic review of the PM

16   NAAQS (62 FR 55201). As part of the process of preparing the PM CD, on April 6-9, 1999, the

17   EPA's National Center for Environmental Assessment (NCEA) hosted a peer review workshop

18   on drafts of key chapters of the CD. The first external review draft CD was reviewed by CASAC

19   and the public at a meeting held on December 2, 1999. Based on CASAC and public comment,

20   NCEA revised the CD and released the second external review draft in April 2001 for review by

21   CASAC and the public at a meeting to be held July 23-24, 2001.

22   This preliminary draft Staff Paper is being provided to the CASAC and the public for

23   comment at that same public meeting. Subsequently, EPA intends to complete staff analyses and

24   to address CASAC and public comments on this draft in a second draft that will then be made

25   available for further review and comment by CASAC and the public.

26

1 ## 1.3 APPROACH

2   The final Staff Paper will rely on the scientific evidence reviewed in the final CD in

3 evaluating the adequacy of the existing PM NAAQS for protection of public health and welfare.

4 The results of comparative air quality and human health risk analyses, as well as analyses

5 examining visibility impairment, will also be presented in the final Staff Paper. The final Staff

6 Paper will include the staff's overall evaluation of the primary and secondary NAAQS and

7 conclusions and recommendations as to whether any revisions are appropriate to address public

8 health and welfare effects associated with fine- and coarse-fraction particles. In so doing, the

9 staff will assess and integrate new scientific and technical findings with information gained in

10 previous reviews in the context of those critical elements that the staff believes should be

11 considered.

12   In conducting various technical analyses, the staff intends to focus separately on fine- and

13 coarse-fraction particles, building upon the conclusions reached in the last review, and taking

14 into account any new information that has become available. More specifically, sufficient data

15 now exist to conduct air quality analyses to characterize spatial and temporal air quality patterns,

16 for example, primarily in terms of $PM_{2.5}$ and $PM_{10-2.5}$ as the indicators for fine- and coarse-

17 fraction particles, respectively, the later referring to particles with a mean aerodynamic diameter

18 between 2.5 and 10 μm. Similarly, the current draft plan for human health risk analyses focuses

19 on analyzing various health effects associated with $PM_{2.5}$, and identifies for further consideration

20 the possibility of also analyzing certain health effects associated with $PM_{10-2.5}$.

21   Beyond this introductory chapter, this preliminary draft Staff Paper is organized into four

22 chapters, with an additional chapter to be added in the next draft presenting staff conclusions and

23 recommendations on the primary and secondary standards. More specifically, Chapter 2 focuses

24 on air quality characterizations, including information on atmospheric concentrations, chemistry,

25 and sources of PM, including, to the extent possible, evaluation of newly available air quality

26 monitoring data, as well as information on the relationship between ambient air quality and

27 human exposure. Chapter 3 presents key information on PM-associated health effects, relying

28 primarily on the review of recent epidemiological and toxicological studies in the draft CD and

29 integrating the new information with findings from previous criteria and NAAQS reviews. Draft

1   plans for a quantitative human health risk analysis are presented for comment in Chapter 4.

2   Information on welfare effects of ambient PM is presented in Chapter 5, together with analyses

3   of data on visibility and draft plans for conducting a focus-group-based assessment of urban

4   visibility impairment.

REFERENCES

Environmental Protection Agency. (2001) Air Quality Criteria for Particulate Matter. Research Triangle Park, NC: Office of Research and Development; report no. EPA/600/P-99/002. March.

U.S. Department of Health, Education and Welfare. (1969) Air Quality Criteria for Particulate Matter. U.S. Government Printing Office, Washington DC, AP-49.

2. AIR QUALITY CHARACTERIZATION

2.1 INTRODUCTION

This chapter defines the various subclasses of particulate matter (PM) and then briefly discusses the physical and chemical properties of PM in the atmosphere, sources of PM, PM measurement methods, and recent PM concentrations and trends. This information is useful for interpreting the available health and welfare effects information and in making recommendations for appropriate indicators for PM. Section 2.2 presents information on the basic physical and chemical properties of classes of PM, and is not substantially different from information contained in the 1996 Criteria Document (EPA, 1996a) and Staff Paper (EPA, 1996b). Section 2.3 presents information on the methods used to measure PM and some of the important considerations in designing these methods. Section 2.4 presents data on PM concentrations, trends, and spatial patterns. Section 2.5 provides information on the temporal variability of PM across daily and monthly time scales. Much of the information in Sections 2.4 and 2.5 is derived from analyses of new data collected by the recently deployed nationwide network of $PM_{2.5}$ monitors. Section 2.6 defines and discusses background levels of PM. Section 2.7 provides national estimates of source emissions. Section 2.8 addresses the relationship between ambient PM levels and human exposure to PM. Finally, Section 2.9 summarizes relevant information on the optical and radiative effects of particles.

2.2 CHARACTERIZATION OF U.S. AMBIENT PARTICULATE MATTER

PM represents a broad class of chemically and physically diverse substances that exist as discrete particles in the condensed (liquid or solid) phase. Particles can be described by size, formation mechanism, origin, chemical composition, atmospheric behavior, and by what is measured by a specific sampling technique. Fine-mode and coarse-mode particles, which are defined in Section 2.2.1.1, are distinct entities with fundamentally different sources and formation processes, chemical composition, atmospheric residence times and behaviors, and transport distances. The 1996 Criteria Document concluded that these differences alone justified consideration of fine-mode and coarse-mode particles as separate pollutants (EPA 1996a, p. 13-

1   3), and this conclusion is reiterated in the new draft Criteria Document (CD, p. 9-1). The

2   fundamental differences between fine-mode and coarse-mode particles are also important

3   considerations in assessing the available health effects and exposure information.

4

5   2.2.1 Particle Size Distributions

6   Particle properties, including their associated health and welfare effects, differ by size.

7   The diameters of atmospheric particles span 5 orders of magnitude, ranging from 0.001

8   micrometers to 100 micrometers (μm).[1] The size and associated composition of particles

9   determine their behavior in the respiratory system (i.e., how far the particles are able to penetrate,

10   where particles are deposited, and how effective the body's clearance mechanisms are in removing

11   them). Furthermore, a particle's size is one of the most important parameters in determining its

12   residence time in ambient air, which is a key consideration in assessing exposure. Particle size is

13   also a determinant of visibility impairment, a welfare effect linked to ambient particles. Particle

14   surface area, number, chemical composition, water solubility, formation processes, and emissions

15   sources all vary with particle size.

16   Two common conventions for classifying particles by size include: (1) modes, based on

17   observed particle size distributions; and (2) cut points, based on the inlet restriction of a specific

18   PM sampling device.

19   2.2.1.1 Modes

20   Based on extensive examinations of particle size distributions in several U.S. locations in

21   the 1970's, Whitby (1978) found that particles display a consistent multi-modal distribution over

22   several physical metrics, such as mass and volume (CD, p. 2-9). These modes are apparent in

23   Figure 2-1, which shows average ambient distributions of particle number, surface area, and

24   volume by particle size. Panel (a) illustrates that most ambient particles are very small, below 0.1

25   μm, while panel (c) indicates most of the particle volume, and therefore most of the mass,

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[1] In this Staff Paper, particle size or diameter usually refers to a normalized measure called aerodynamic diameter. Most ambient particles are irregularly shaped rather than perfect spheres. The aerodynamic diameter of any irregular shaped particle is defined as the diameter of a spherical particle with a material density of 1 g/cm^3 and the same settling velocity as the irregular shaped particle. Particles with the same physical size and shape but different densities will have different aerodynamic diameters (CD, p. 2-3).
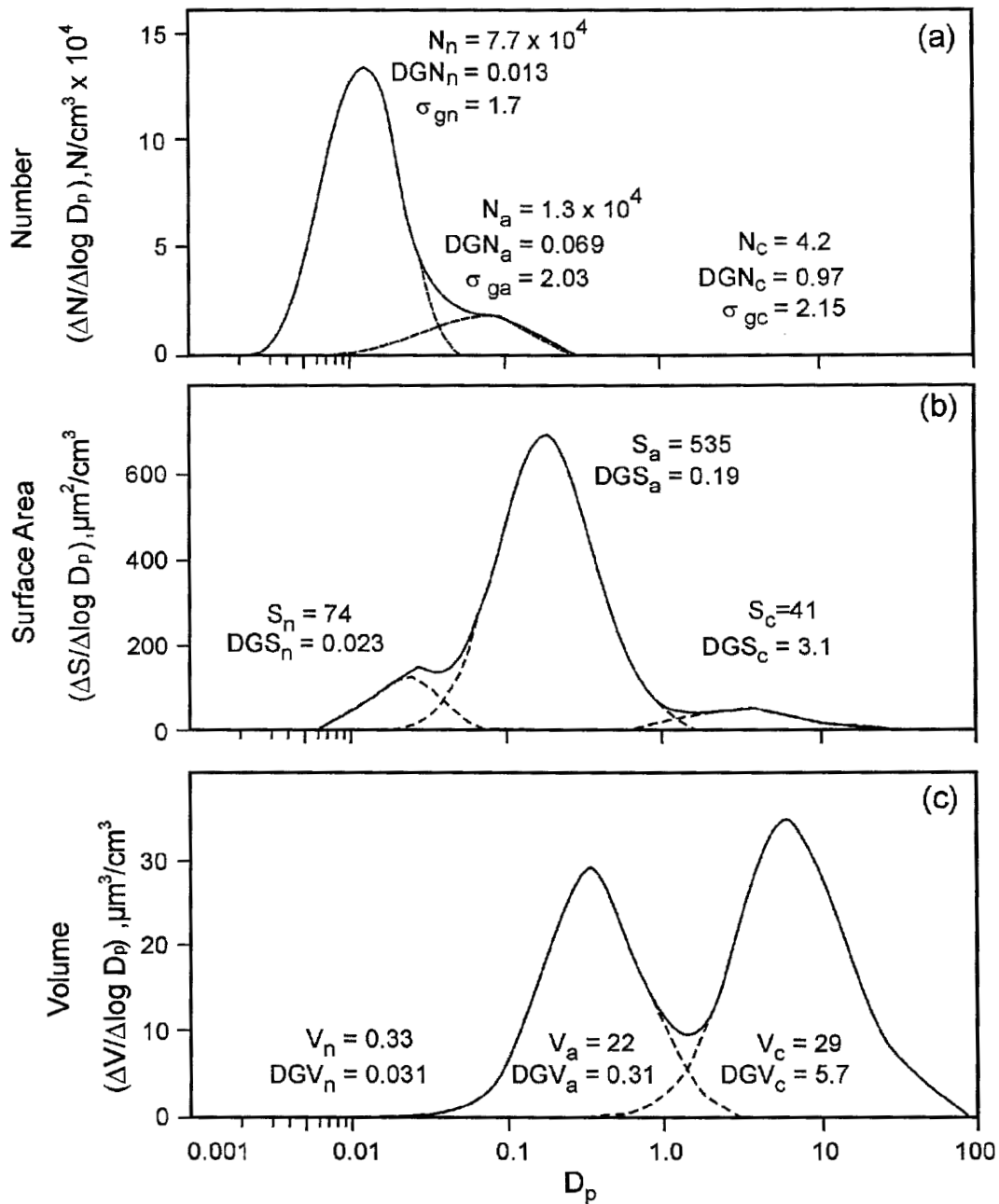
Figure 2-1. Distribution of coarse [c], accumulation [a], and nuclei or ultrafine [n], mode particles by three characteristics: Panel (a) number [N], Panel (b) surface area [S], and Panel (c) volume [V] for the grand average continental size distribution. D_p = geometric diameter; DGN = geometric mean diameter by number; DGS = geometric mean diameter by surface area; DGV = geometric mean diameter by volume.

Source: Whitby (1978); CD, page 2-7.

1 is found in particles larger than 0.1 µm. The surface area distribution in panel (b) peaks around

2 0.2 µm (CD, p. 2-5). Distributions may vary across locations, conditions, and time due to

3 differences in sources, atmospheric conditions, and topography.

4   As illustrated in panel (c) of Figure 2-1, volume distributions measured in ambient air in

5 the United States are almost always found naturally to be bimodal, with an intermodal minimum

6 between 1 and 3 µm (CD, p. 2-6). The distribution of particles that are mostly larger than this

7 minimum is termed "coarse mode," and the distribution of particles that are mostly smaller than

8 the minimum is termed "fine mode." Fine-mode particles are separated into two sub-modes:

9 "accumulation mode" and "nuclei mode" (also known as "ultrafines"). The accumulation mode

10 and the nuclei mode are apparent as the leftmost peaks in the number and surface area

11 distributions in Figure 2-1, whereas the accumulation mode is apparent as the leftmost peak in the

12 volume distribution. Since nuclei-mode particles have relatively low mass and grow rapidly into

13 accumulation-mode particles, they are not commonly observed as a separate mode in volume or

14 mass distributions. Exceptions include clean or remote areas with low PM concentrations, and

15 areas near freshly generated fine-mode particles such as freeways and intersections with heavy

16 automobile traffic (CD, pp. 2-10 and 2-17).

17 **2.2.1.2 Sampler Cut Points**

18   Another set of particle size classifications is derived from the characteristics of ambient

19 particle samplers. Particle samplers typically use size-selective air inlets that are defined by their

20 50 percent cut point, which is the cut point at which 50 percent of particles of a specified diameter

21 are captured by the inlet. The usual notation for these definitions is "PM_x", where x refers to

22 measurements with a cut point of x µm aerodynamic diameter. Because of the overlap in the

23 distributions of ambient particles, no single cut point can precisely separate fine-mode and coarse-

24 mode particles. The objective of size-selective sampling is usually to measure particle size

25 fractions with some special relationship to human health impacts, visibility impairment, or

26 emissions sources.

27   The EPA has historically defined indicators of PM for national ambient air quality

28 standards (NAAQS) using various cut points. Figure 2-2 presents an idealized distribution of

29 ambient PM showing the fractions collected by size-selective samplers. Prior to 1987, the

1   indicator for the PM NAAQS was total suspended particulate matter (TSP), and was defined by

2   the design of the High Volume Sampler (hivol).[2] As shown in Figure 2-2, TSP includes particle

3   diameters less than 40 μm. When EPA established new PM standards in 1987, the selection of

4   PM_{10} as an indicator was intended to focus regulatory concern on particles small enough to enter

5   the thoracic region of the lungs. In 1997, EPA established a new standard for a fraction of fine-

6   mode particles based in part on epidemiological studies that used $PM_{2.5}$ concentrations as an

7   exposure index. Figure 2-2 shows the distribution of particles captured by the PM_{10} Federal

8   Reference Method (FRM) sampler[3] and the $PM_{2.5}$ FRM sampler[4].

9   The common PM measurement indicators used in this Staff Paper are summarized in Table

10   2-1. Note that the terms "fine fraction" and "coarse fraction" are used interchangeably with $PM_{2.5}$

11   and $PM_{10-2.5}$, respectively, to refer to specific portions of the fine and coarse modes collected by

12   size selective samplers.

13

14   **2.2.2   Sources and Formation Processes**

         In most locations, a variety of activities contribute to PM concentrations. Fine-mode and

coarse-mode particles generally have distinct sources and formation mechanisms although there is

some overlap. Coarse-mode particles are primary particles, meaning they are emitted directly as

particles. Most coarse-mode particles result from mechanical disruption such as crushing,

grinding, evaporation of sprays, or dust resuspension. Specific sources include construction and

demolition activities, sea spray, and resuspension of settled dust from soil surfaces and roads (CD,

p. 3-34). The amount of energy required to break down primary particles into smaller particles

normally limits coarse-mode particle sizes to greater than 1.0 μm diameter (EPA 1996a, p. 13-7).

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[2] 40 CFR Part 50, Appendix B.

[3] 40 CFR Part 50, Appendix J.

[4] 40 CFR Part 50, Appendix L.
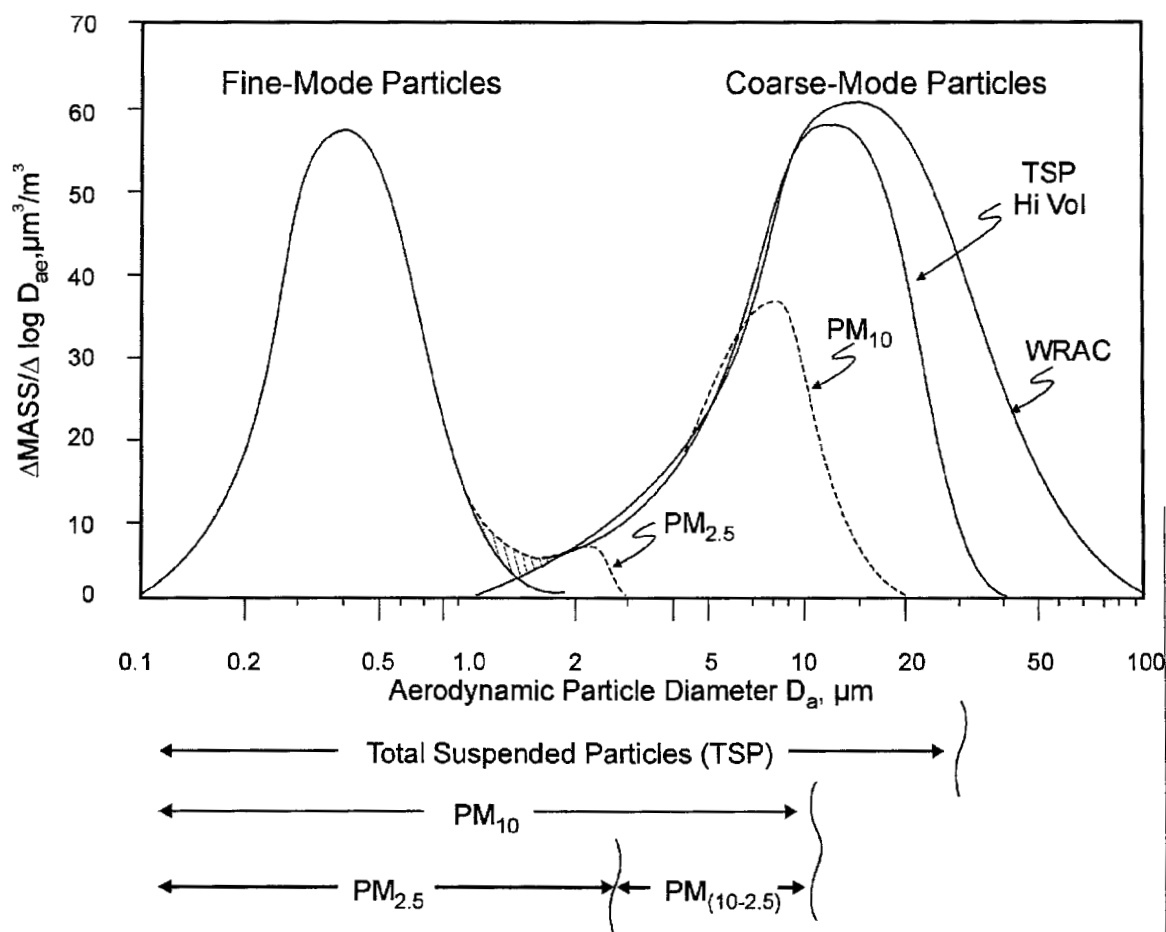
Figure 2-2. An idealized distribution of ambient particulate matter showing fine-mode particles and coarse-mode particles and the fractions collected by size-selective samplers. (WRAC is the Wide Range Aerosol Classifier which collects the entire coarse mode.) Note that this idealized distribution is truncated at a diameter of 0.1 μm, such that it does not include the ultrafine fraction.

Source: Adapted from Wilson and Suh (1997); CD, page 2-11.

Some combustion-generated particles such as fly ash are also found in the coarse mode.

Table 2-1. Particle Size Fraction Terminology Used in Staff Paper

Term	Description
Size Distribution Modes	
Coarse-Mode Particles	The distribution of particles larger than the intermodal minimum in volume or mass distributions, which generally occurs between 1 and 3 μm.
Fine-Mode Particles	The distribution of particles smaller than the intermodal minimum in volume or mass distributions, which generally occurs between 1 and 3 μm. Particles in this mode are the most numerous and represent the most surface area.
Accumulation-Mode Particles	A subset of fine-mode particles with diameters above about 0.1 μm.
Nuclei-Mode Particles ("ultrafines")	A subset of fine-mode particles with diameters below about 0.1 μm.
Sampling Measurements	
Total Suspended Particles (TSP)	Particles measured by a high volume sampler as described in 40 CFR Part 50, Appendix B. This sampler has a cut point of aerodynamic diameters that varies between 25 and 40 μm depending on wind speed and direction.
PM_{10}	Particles measured by a sampler that contains a size fractionator (classifier) designed with an effective cut point of 10 μm aerodynamic diameter. This measurement includes the fine mode and part of the general coarse mode and is an indicator for thoracic particles (i.e., particles that penetrate to the tracheo-bronchial and the gas-exchange regions of the lung).
$PM_{2.5}$ "fine fraction"	Particles measured by a sampler that contains a size fractionator (classifier) designed with an effective cut point of 2.5 μm aerodynamic diameter. The collected particles include most of the fine mode. A small portion of the coarse mode may be included depending on the sharpness of the sampler efficiency curve and the size of coarse mode particles present.
$PM_{(10-2.5)}$ "coarse fraction"	Particles measured directly using a dichotomous sampler or subtraction of particles measured by a $PM_{2.5}$ sampler from those measured by a PM_{10} sampler. This measurement is an indicator for the fraction of coarse-mode thoracic particles (i.e., particles that penetrate to the tracheo-bronchial and the gas-exchange regions of the lung).

1   Directly emitted particles are also found in the fine mode, the most common being nuclei-

2   mode particles emitted as combustion-related vapors that rapidly condense. They originate from

3   fuel combustion (from vehicles, power generation, and industrial facilities), residential wood

4   burning, and agricultural and silvicultural burning. However, the majority of fine-mode mass is

5   attributable to secondary particles, formed in the atmosphere from gases (CD, p. 2-20). Fine-

6   mode particles are usually formed from gases in three ways: (1) nucleation (i.e., gas molecules

7   coming together to form a new particle); (2) condensation of gases onto existing particles; and (3)

8   coagulation of particles (CD, p. 2-2). Gas phase material condenses preferentially on smaller

9   particles, and the rate constant for coagulation of two particles decreases as the particle size

10   increases. Therefore, nuclei-mode particles grow into the accumulation mode, but accumulation-

11   mode particles do not grow into the coarse mode (CD, p. 2-16). Examples of secondary particle

12   formation include: (1) the conversion of sulfur dioxide (SO_2) to sulfuric acid (H_2SO_4) droplets

13   that further react with ammonia (NH_3) to form sulfate (ammonium sulfate $((NH_4)_2SO_4)$ or

14   ammonium acid sulfate $(NH_4HSO_4))$ particles; (2) the conversion of nitrogen dioxide (NO_2) to

15   nitric acid (HNO_3) which reacts further with ammonia to form ammonium nitrate (NH_4NO_3)

16   particles; and (3) reactions involving volatile organic compounds (VOC) yielding organic

17   compounds with low ambient temperature vapor pressures that nucleate or condense on existing

18   particles to form secondary organic particles (CD, p. 2-21).

19

20   **2.2.3   Chemical Composition**

21   Based on studies conducted in most parts of the U.S., the draft CD reports that coarse-

22   mode particles are composed primarily of crustal materials such as calcium, aluminum, silicon,

23   magnesium, and iron. Some organic materials such as pollen, spores, and plant and animal debris

24   are also found predominantly in the coarse mode (CD, p. 2-19). Fine-mode particles are

25   composed primarily of sulfate, nitrate, ammonium, and hydrogen ions; elemental carbon,

26   secondary organic compounds and some primary organic compounds; and certain transition

27   metals deriving primarily from combustion processes..

28   Some components, such as potassium and nitrate, may be found in both the fine and

29   coarse particle modes, but different sources or mechanisms contribute to their existence in each

1   mode. Potassium in coarse-mode particles comes from soil. Potassium in fine-mode particles

2   comes from emissions of burning wood or cooking meat. Nitrate in fine-mode particles comes

3   primarily from the reaction of gas-phase nitric acid with gas-phase ammonia to form ammonium

4   nitrate particles. Nitrate in coarse-mode particles comes primarily from the reaction of gas-phase

5   nitric acid with pre-existing coarse-mode particles (CD, p. 2-19).

6   Many ambient particles also contain water (particle-bound water) as a result of equilibrium

7   of water vapor with water bound to hygroscopic particles (CD, p. 2-28). Particle-bound water

8   influences the size of particles and in turn their aerodynamic and light scattering properties.

9   Studies of the change in particle size with changes in relative humidity (RH) suggest that a small

10   fraction of accumulation-mode particles (with a dry diameter smaller than 1 μm) will be larger

11   than 1 μm in diameter at RH below 60%, but a larger fraction will grow above 1 μm for RH

12   above 80% (CD, p. 2-39). The amount of the increase in particle size with increasing RH is

13   dependent on the particle's chemical composition (CD, p. 4-91). Particles containing inorganic

14   salts and acids are more hygroscopic than particles composed primarily of organic species.

15

16   **2.2.4   Fate and Transport**

17   Fine-mode and coarse-mode particles typically exhibit different behavior in the

18   atmosphere. These differences affect several exposure considerations including the

19   representativeness of central-site monitored values and the behavior indoors of particles that were

20   formed outdoors. The ambient residence time of atmospheric particles varies with size. Coarse-

21   mode particles can settle rapidly from the atmosphere with lifetimes from a few seconds to hours,

22   and their spatial impact is limited because they tend to fall out of the air in the downwind area

23   near their emission point. Larger coarse-mode particles are not readily transported across urban

24   or broader areas, because they are generally too large to follow air streams, and they tend to be

25   easily removed by impaction on surfaces. Smaller-sized coarse-mode particles can have longer

26   lives and longer travel distances, especially in extreme circumstances, such as dust storms (CD, p.

27   2-30).

28   Fine-mode particles are kept suspended by normal air motions and have low surface

29   deposition rates. Because they grow rapidly into the accumulation mode, the subset of nuclei-

1 mode particles have a very short life, on the order of minutes to hours. Nuclei-mode particles are

2 also small enough to be removed through diffusion to falling rain drops (CD, p. 2-32).

3 Accumulation-mode particles, which do not grow into the coarse mode, can be transported

4 thousands of kilometers and remain in the atmosphere for days to weeks. Accumulation-mode

5 particles are removed from the atmosphere primarily by cloud processes. They serve as

6 condensation nuclei for cloud droplet formation and eventually fall as rain drops. However,

7 accumulation-mode particles are not effectively removed from the atmosphere by falling rain (CD,

8 p. 2-30).

9   Because fine-mode particles remain suspended for days to weeks, and travel much farther

10 than coarse-mode particles, fine-mode particles are theoretically likely to be more uniformly

11 dispersed at urban scales than coarse particles. In contrast, coarse-mode particles tend to exhibit

12 more elevated concentrations near sources (EPA 1996a, p. 13-15).

13   The characteristics of nuclei-mode, accumulation-mode, and coarse-mode particles that

14 were discussed in the preceding sections are summarized in Table 2-2.

15

16 **2.3   PM MEASUREMENT METHODS**

17   The draft CD indicates that the methods used to measure PM are important to

18 understanding population exposure to PM, evaluating health risks, and developing risk

19 management strategies. Because PM is not a homogeneous pollutant, measuring and

20 characterizing particles suspended in the atmosphere is a significant challenge, and there is no

21 perfect method for every application.[5] Measurements include particle mass, composition, and

22 particle number. Most instruments collect PM by drawing a controlled volume of ambient air

23 through a size-selective inlet, usually defined by the inlet's 50 percent cut point. Often used

24 measurements or indicators of fine-mode particles include $PM_{2.5}$, $PM_{1.0}$, British or black smoke

25 (BS), coefficient of haze (COH), sulfates, acids, and PM_{10} (in areas dominated by fine-mode

26 particles). Measurements of coarse-mode particles include $PM_{10-2.5}$, $PM_{15-2.5}$, and PM_{10} (in areas

27 dominated by coarse-mode particles).

---

[5] Refer to EPA 1996a, Chapter 4 and draft CD Chapter 2 for more comprehensive assessments of particle measurement methods.

Table 2-2. Comparison of Ambient Particles: Fine Mode (Nuclei Mode plus Accumulation Mode) and Coarse Mode

	Fine-Mode Particles		Coarse-Mode Particles
	Nuclei Mode	Accumulation Mode	
Aerometric Diameter	< 0.1 µm	0.1 – 3.0 µm	> 1.0 µm
Formed from:	Combustion, high temperature processes and atmospheric reactions		Break-up of large solids/droplets
Formed by:	Nucleation Condensation Coagulation	Condensation Coagulation Evaporation of fog and cloud droplets in which gases have dissolved and reacted	Mechanical disruption (crushing, grinding, abrasion of surfaces) Evaporation of sprays Suspension of dusts Reactions of gases in or on particles
Composed of:	Sulfate, SO_4 Elemental carbon Metals compounds (Pb, Cd, V, Ni, Cu, Zn, Mn, Fe, K, etc.) Organic compounds with very low, saturation vapor pressure at ambient temperature	Sulfate Nitrate, NO_3 Ammonium, NH_4^+ Hydrogen ion, H^+ Elemental carbon, Large variety of organic compounds Metal compounds Particle-bound water	Suspended soil or street dust Fly ash from uncontrolled combustion of coal, oil, wood Nitrates/chlorides from HNO_3/HCl Oxides of crustal elements (Si, Al, Ti, Fe, Mg) $CaCO_3$, NaCl, sea salt Pollen, mold, fungal spores Plant/animal fragments Tire, brake pad, and road wear debris
Solubility:	Probably less soluble than accumulation mode	Largely soluble, hygroscopic and deliquescent	Largely insoluble and non-hygroscopic
Sources:	Combustion of coal, oil, gasoline, diesel fuel, wood Atmospheric transformation of SO_2 and some organic compounds High temperature processes, smelters, steel mills, etc.	Combustion Atmospheric transformation products of NO_x, SO_2, and organic compounds including biogenic organic species (e.g., terpenes) High temperature processes Volcanic activity Wildfires	Resuspension of industrial dust and soil tracked onto roads and streets Suspension from disturbed soil (e.g., farming, mining, unpaved roads) Construction and demolition Uncontrolled coal and oil combustion Ocean spray Biological sources
Atmospheric half-life:	Minutes to hours	Days to weeks	Minutes to hours
Removal Processes:	Grows into accumulation mode Scavenging by falling rain drops	Forms cloud droplets and rains out Dry deposition	Dry deposition by fallout Scavenging by falling rain drops
Travel distance:	<1 to 10s of km	100s to 1000s of km	<1 to 10s of km (100s to 1000s in dust storms)

Source: Adapted from Wilson and Suh (1997); CD, p. 2-35.

1   PM mass can be measured directly, by gravimetric methods, or indirectly using methods

2   that rely on the physical properties of particles. The most common direct measurement methods

3   include filter-based methods where ambient aerosols are collected for a specified period of time

4   (e.g., 24 hours) on filters that are weighed to determine mass. Examples include the Federal

5   Reference Method monitors for $PM_{2.5}$ and PM_{10}. Dichotomous samplers contain a separator that

6   splits the air stream from a PM_{10} inlet into two streams so that both fine and coarse fraction

7   particles can be collected on separate filters. With this approach a fraction of the fine-mode

8   particles are collected with the coarse-mode particles.

9   Another widely used gravimetric method is the Tapered Element Oscillating Microbalance

10   (TEOM®) sensor, consisting of a replaceable filter mounted on the narrow end of a hollow

11   tapered quartz tube. The air flow passes through the filter, and the aerosol mass collected on the

12   filter causes the characteristic oscillation frequency of the tapered tube to change in direct relation

13   to particle mass. This approach allows mass measurements on a near-continuous basis (every few

14   minutes).

15   Other methods that produce near-continuous PM measurements include beta attenuation

16   sampler and the Continuous Ambient Mass Monitor (CAMM). Beta attenuation (or beta gauge)

17   samplers determine the mass of particles deposited on a filter by measuring the absorption of

18   electrons generated by a radioactive isotope. The absorption varies with the mass of the particles.

19   The CAMM measures the pressure drop increase that occurs in relation to particle loading on a

20   membrane filter.

21   PM has also been characterized in the U.S. and abroad by indirect filter-based optical

22   methods that rely on the light scattering or absorbing properties of both suspended PM and PM

23   collected on a filter.[6] These include BS and COH, as well as estimates derived from visibility

24   measurements. In locations where they are calibrated to standard mass units, these indirect

25   measurements can be useful surrogates for particle mass. The BS method typically involves

26   impacting samples from a 4.5 µm inlet onto white filter paper where blackness of the stain is

27   measured by light absorption. Smoke particles composed of elemental carbon (EC) typically

---

[6] See Section 2.8 of this chapter for a discussion of the optical properties of PM.

1	make the largest contribution to stain darkness. Since the mix of ambient particles varies widely
2	by location and time of year, the correlation between BS measurements and PM mass are highly
3	site- and time-specific. COH is determined using a light transmittance method. This involves
4	impacting samples from a 5.0 μm inlet onto filter tape where the opacity of the resulting stain is
5	determined. This technique is somewhat more responsive to non-carbon particles than the BS
6	method. Nephelometers measure the light scattered by ambient aerosols in order to calculate light
7	extinction. This method results in measurements that can correlate well with the mass of fine-
8	mode particles below 2 μm diameter.
9	There are a variety of methods used to identify and describe the characteristic
10	components of ambient PM. X-ray fluorescence (XRF) is a commonly used laboratory technique
11	for analyzing the elemental composition of primary particles deposited on filters Wet chemical
12	analysis methods, such as ion chromatography (IC) and automated colorimetry (AC) are used to
13	measure ions such as nitrate (NO_3^-), sulfate (SO_4^-), chloride (Cl^-), ammonium (NH^+), sodium
14	(Na^+), and phosphate (PO_4^{3-}).
15	There are several methods for separating organic carbon (OC) and elemental carbon (EC)
16	in ambient samples. Thermal/optical reflectance (TOR) and thermal manganese oxidation (TMO)
17	have been commonly applied in aerosol studies in the United States. Still another method is the
18	thermal/optical transmission (TOT) method. This method is similar to TOR and yields
19	comparable estimates of total carbon, but gives a different split between OC and EC. Monitoring
20	methods capable of separately measuring sulfate, nitrate, and carbon particles on a near-
21	continuous basis are currently under development..
22	The presence of semi-volatile PM components and sampling in extreme climate conditions
23	present special challenges for designing measurement methods. Accurate measurement of fine-
24	mode particles is particularly difficult when the relative humidity is high, or when winds cause
25	high ambient concentrations of wind-blown soil. In these conditions, a significant amount of
26	either fine-mode or coarse-mode material may be found in the inter-modal region between 1.0 and
27	3 μm diameter. The draft CD suggests that under these conditions a better measurement of fine-
28	mode particles could be obtained by removing all or most particle-bound water, measuring PM at
29	a constant relative humidity, and using a cut point of 1.0 μm rather than 2.5 μm diameter (CD, p.

1   2-40). All continuous monitoring methods require removal of particle-bound water prior to mass

2   measurement. However, heating the inlet stream to a constant temperature to keep moisture in

3   the vapor phase can have the negative effect of removing a portion of the PM compounds that

4   have equilibrium vapor pressures that are higher than typical ambient temperatures, and can

5   chemically degrade some organic compounds. Newer techniques use diffusion drying to remove

6   water vapor, leading to vaporization of particle-bound water without heating.

7   In addition to particle mass and composition, the number of ambient particles can also be

8   measured. Recently there has been increasing interest in examining the relationship between the

9   number of ambient particles and health effects. A nano-scanning mobility particle sizer (NSMPS)

10   counts particles in the 0.003 to 0.15 μm range. A standard scanning mobility particle sizer

11   (SMPS) counts particles in the 0.01 to 1 μm range, and a laser particle counter (LPC) counts

12   particles in the 0.1 to 2 μm range. An aerodynamic particle sizer measures particles in the 0.7 to

13   10 μm range. These techniques have not yet been widely used in health effects studies.

14

15   **2.4   PM CONCENTRATIONS, TRENDS, AND SPATIAL PATTERNS**

16   This section provides analysis of the latest available PM air quality data, including PM

17   levels, composition, spatial patterns, and temporal patterns. Only recently has a full year of mass

18   concentration data from a nationwide network of $PM_{2.5}$ Federal Reference Method (FRM)

19   monitors been available, and analyses of those data are presented here. Readers should be

20   cautioned not to draw conclusions regarding the attainment or nonattainment status from a single

21   year of PM monitoring data. EPA regulations, in 40 CFR Part 50, Appendix N, require 3 years of

22   monitoring data and specify minimum data completeness requirements for data used to make

23   decisions regarding attainment status. Not all PM FRM monitors that were operated in 1999

24   recorded valid PM measurements for all four calendar quarters. In the figures that follow, data

25   completeness is illustrated by the size of the circles on the map, with smaller circles indicating

26   relatively incomplete data for the year. Additional $PM_{2.5}$ data are presented from other long-term

27   monitoring efforts, including data from the network for Interagency Monitoring of Protected

28   Visual Environments (IMPROVE) and from the California Air Resources Board, which are not

29   directly comparable to the FRM monitor data.

1 **2.4.1 PM_{10}**

2   State and local air pollution control agencies have been collecting PM_{10} mass

3 concentration data using EPA-approved FRM samplers and reporting these data to EPA's publicly

4 available Aerometric Information Retrieval System (AIRS) data base since mid-1987.[7] PM_{10} data

5 from 1999 are shown in Figures 2-3a and 2-3b. Figure 2-3a shows the PM_{10} annual mean

6 concentrations, and Figure 2-3b shows the second highest 24-hour average concentrations. Most

7 areas of the country had concentrations below the level of the annual mean PM_{10} standard (50

8 $\mu g/m^3$). Exceptions include central South Carolina, Puerto Rico, and several places in the

9 southwestern U.S. and central California. Most areas of the country also had concentrations

10 below the level of the 24-hour standard (150 $\mu g/m^3$), with exceptions mostly in the western U.S.

11   In the 1998 National Air Quality and Emissions Trends Report (EPA 2000b), EPA

12 examined national and regional PM_{10} trends for the 10-year period from 1989 to 1998. Figure 2-4

13 shows the national trend and the trend in each EPA region. The figure shows approximately a 25

14 percent decline in concentrations over the 10 year period with regional declines in the eastern

15 U.S. ranging from 18 to 21 percent, and declines in the western U.S. ranging from 31 to 38

16 percent. In the national trend and in several regions, the declines appearing to level off in more

17 recent years. Figure 2-5 shows the national 10-year trend in annual mean PM_{10} concentrations for

18 906 sites broken down into rural, suburban, and urban locations. Rural levels are significantly

19 lower than suburban and urban levels, but all three classifications show a similar decline of about

20 25 percent.

---

[7] Based in part on this data, EPA has designated areas of the country that are not attaining PM_{10} standards. As of July 2000 there were a total of 66 areas classified as moderate or serious nonattainment areas, mostly in the western U.S., with fewer in heavily populated or industrialized eastern areas. See designated nonattainment areas at www.epa.gov/oar/oaqps/greenbook.
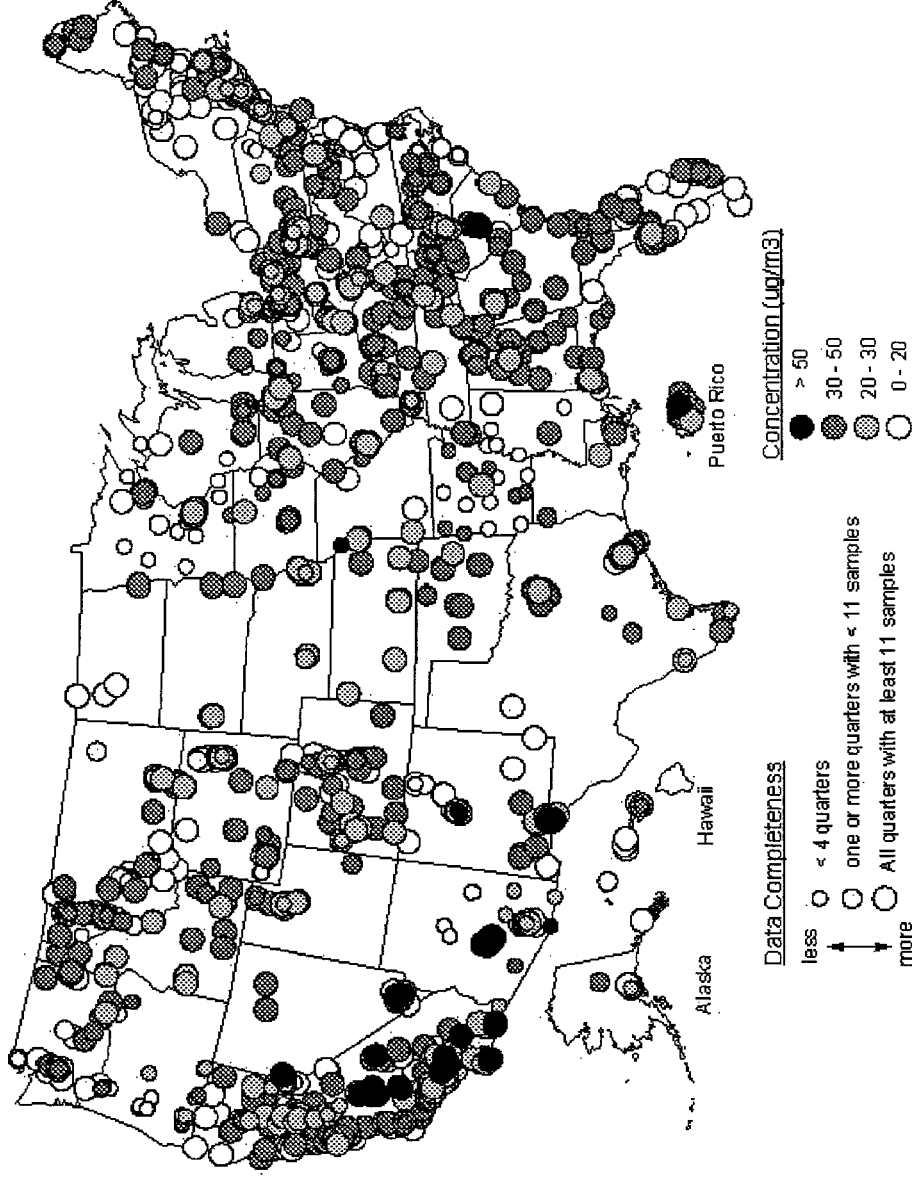
Figure 2-3a. 1999 annual mean PM₁₀ concentrations (µg/m³)

Source: Fitz-Simons et al. (2000)
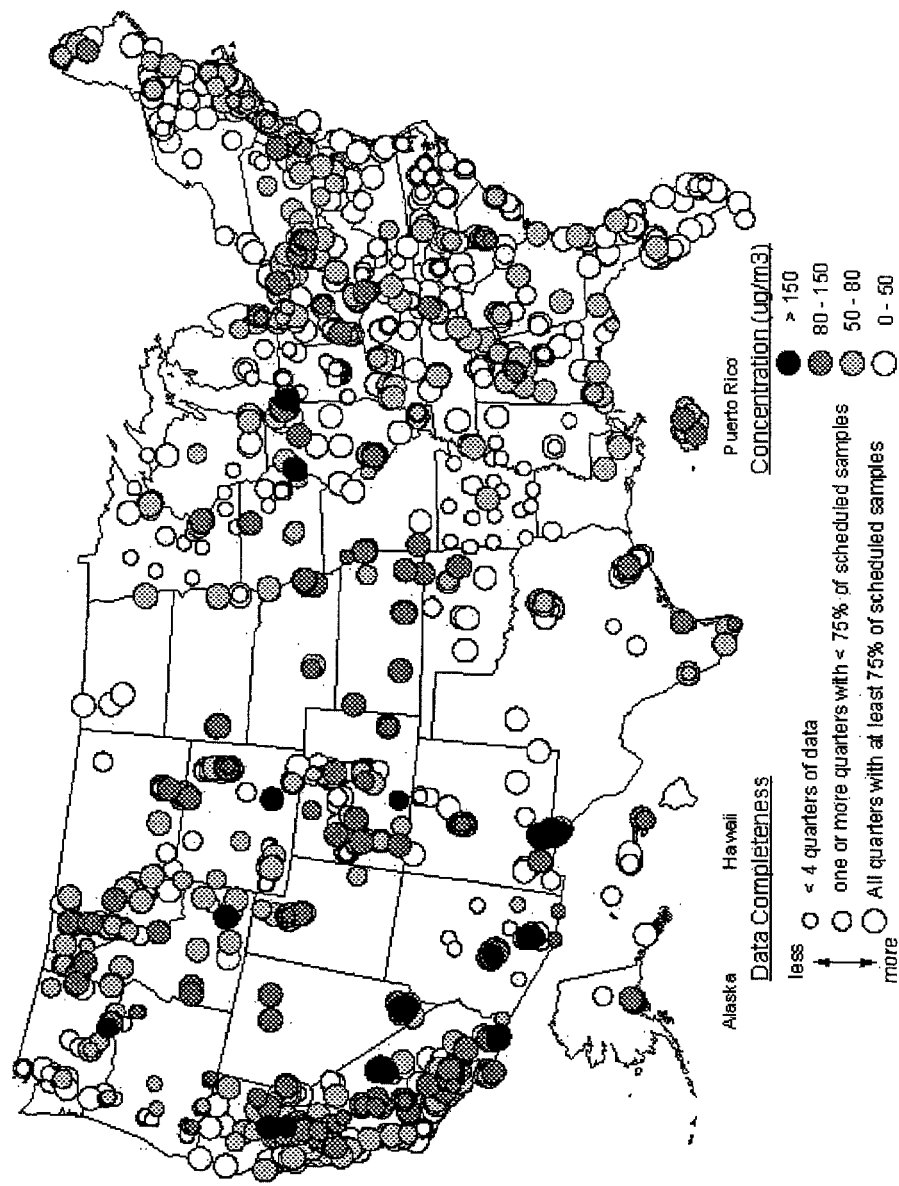
Figure 2-3b. 1999 2nd highest 24-hour average PM₁₀ concentrations (μg/m³)

Source: Fitz-Simons et al. (2000)

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2-17   *Do Not Cite or Quote*
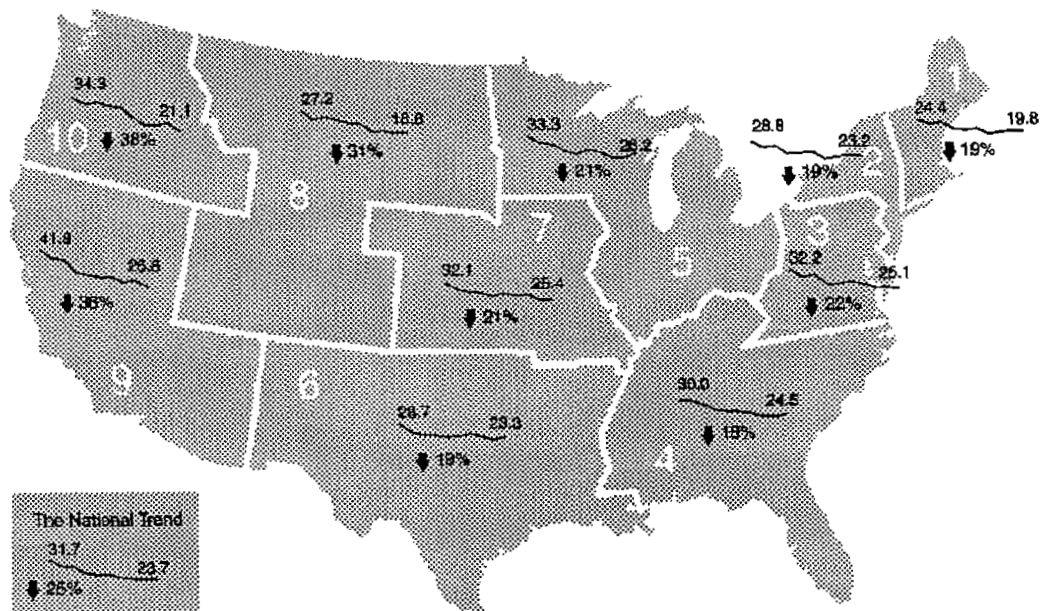
Alaska is in EPA Region 10; Hawaii, EPA Region 9; and Puerto Rico, EPA Region 2.
Concentrations are μg/m3.

Figure 2-4. Trend in annual mean PM$_{10}$ concentrations by EPA region, 1989-1998 (μg/m^3).

Source: Environmental Protection Agency (2000b)
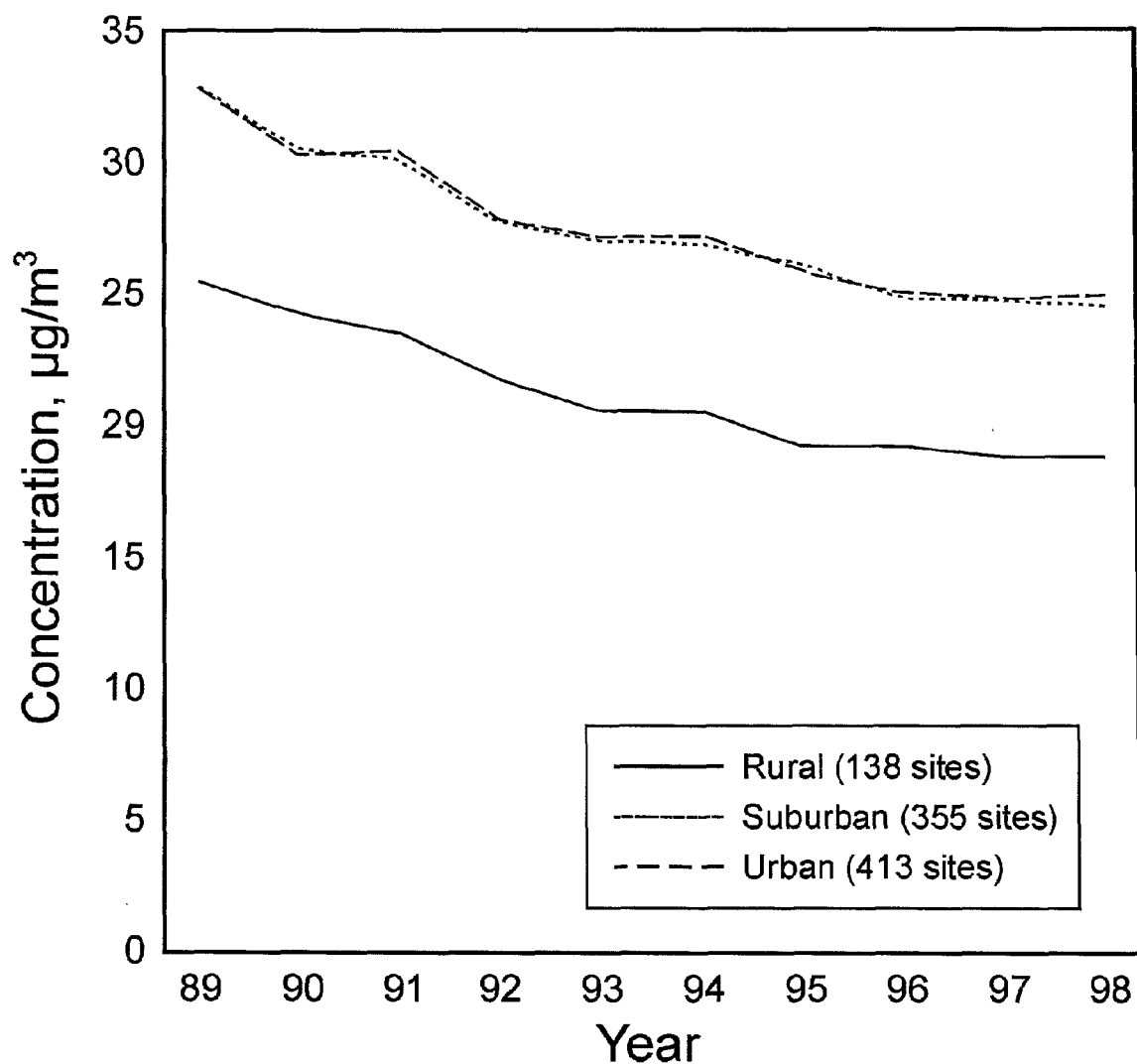
Figure 2-5. Nationwide trend in annual mean PM_{10} concentrations for rural, suburban, and urban locations from 1989 through 1998.

Source: Environmental Protection Agency (2000b)

1   **2.4.2 $PM_{2.5}$**

2   Following the 1997 PM NAAQS revisions, which set a new NAAQS for $PM_{2.5}$, EPA led a

3   nationwide effort to deploy and operate over 1000 $PM_{2.5}$ monitors. These monitors use the

4   Federal Reference Method (FRM), which if followed assures that PM data are collected using

5   standard equipment, operating procedures, and data handling techniques.[8] The first year of data

6   collected by that network has been analyzed by Fitz-Simons et al. (2000). About 54 percent of

7   the monitors had fewer than 11 valid samples recorded in every quarter, the minimum number

8   generally required for calculating quarterly means.[9]

9   Figure 2-6a depicts nationwide annual mean $PM_{2.5}$ concentrations from the FRM network.

10   Many locations in the eastern U.S. and in California were above 15 $\mu g/m^3$. Annual mean

11   concentrations were above 20 $\mu g/m^3$ in several major urban areas throughout the eastern U.S.,

12   including Pittsburgh, Cleveland, Atlanta, Chicago, St. Louis, and in Los Angeles and the central

13   valley of California. Sites in the central and western mountain regions of the U.S. had generally

14   low annual mean concentrations, most below 10 $\mu g/m^3$.

15   Figure 2-6b depicts nationwide 98th percentile 24-hour average $PM_{2.5}$ concentrations from

16   the FRM monitor network. Concentrations above 65 $\mu g/m^3$ were relatively rare in the eastern

17   U.S., but more prevalent in California. Values in the 40 - 65 $\mu g/m^3$ range were more common in

18   the eastern U.S. and on the west coast, but relatively rare in the central and western mountain

19   regions. In these regions, the 98th percentile 24-hour average concentrations were more typically

20   below 40 $\mu g/m^3$, with many below 30 $\mu g/m^3$.

21   There are limited data available on longer-term trends in $PM_{2.5}$ concentrations. Long-term

22   $PM_{2.5}$ data collected by the California Air Resources Board show that from 1990 to 1995 annual

23   average $PM_{2.5}$ concentrations decreased about 50% in the South Coast Air Basin, 35% in the San

24   Joaquin Valley, 30% in the San Francisco Bay Area, and 35% in the Sacramento Valley

25   (Dolislager and Motallebi, 1999). $PM_{2.5}$ data also have been collected continuously since 1994 as

26   part of a children's health study in twelve communities in southern California (Taylor et al.,

---

[8] See 40 CFR Parts 50 and 58 for monitoring program requirements.

[9] See 40 CFR Part 50, Appendix N, Section 2.0 Comparisons with the $PM_{2.5}$ standards.
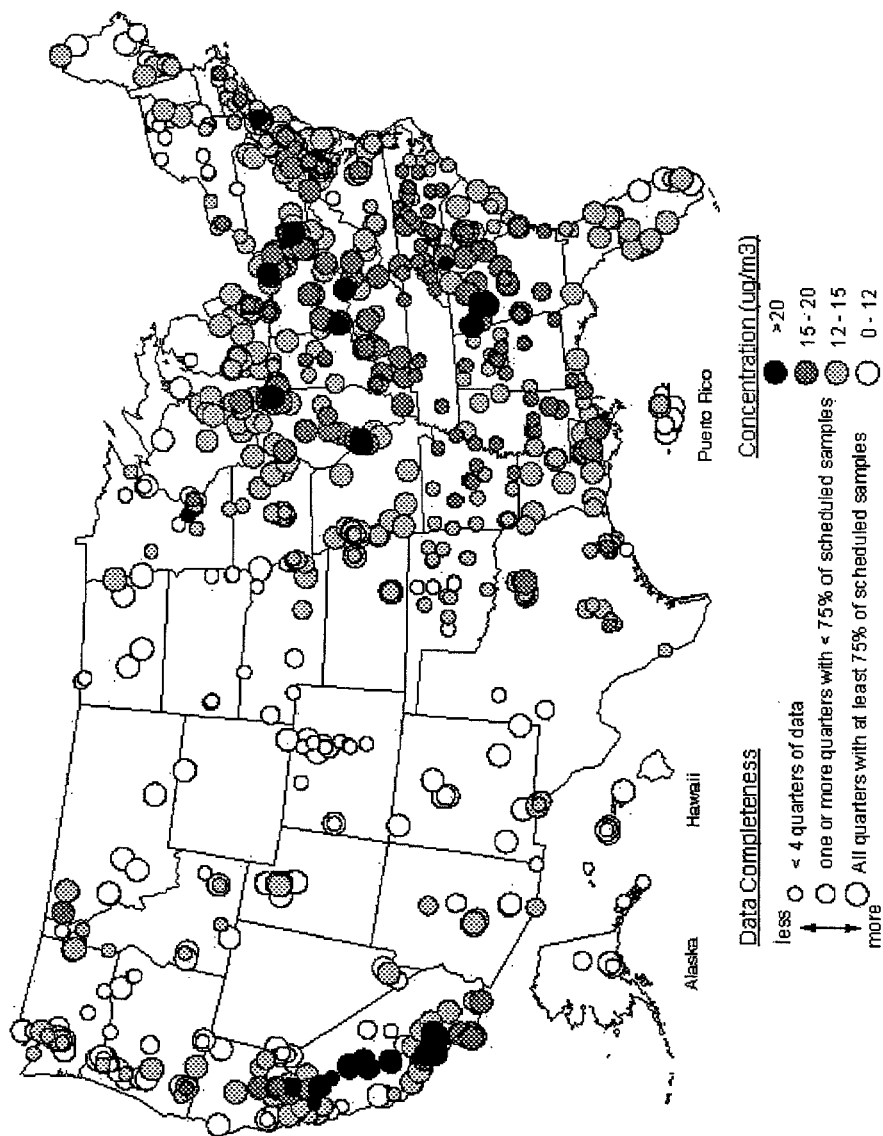
Figure 2-6a. 1999 annual mean PM$_{2.5}$ concentrations (μg/m^3)

Source: Fitz-Simons et al. (2000)
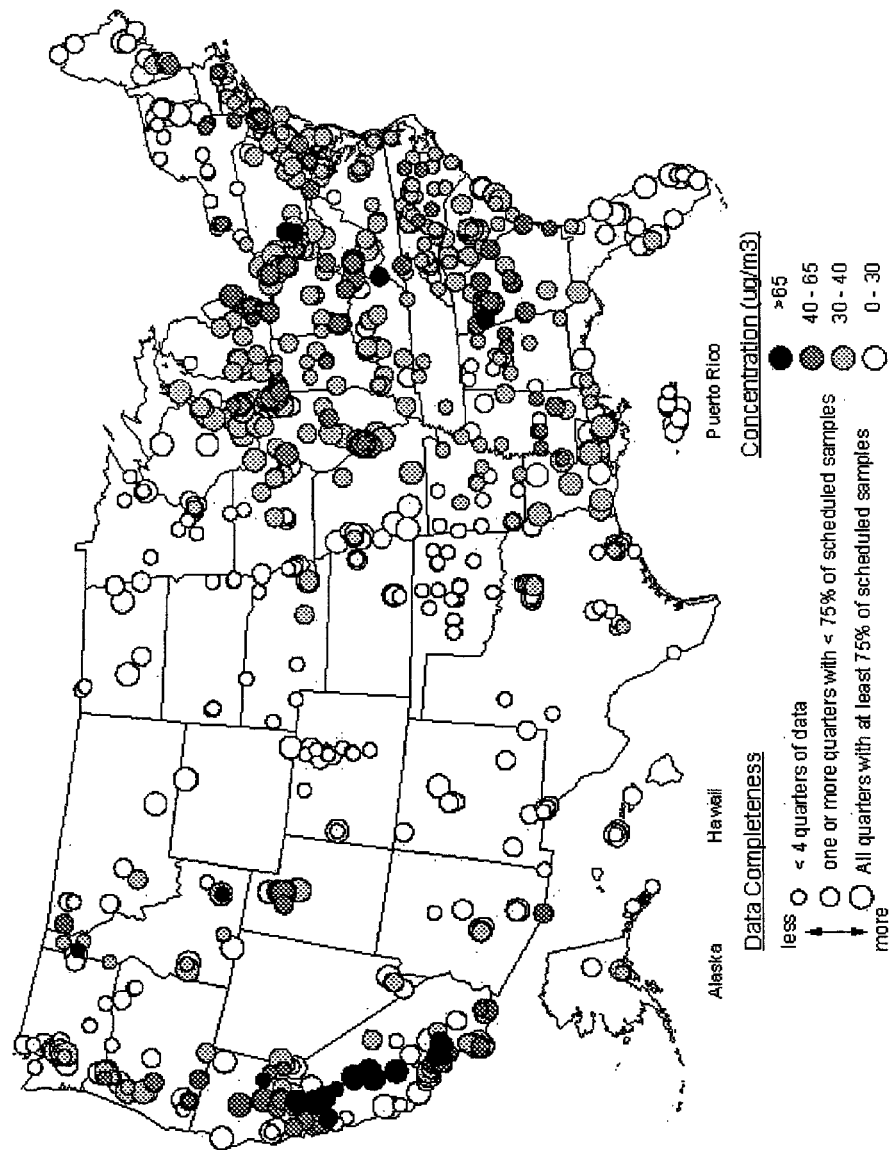
Figure 2-6b. 1999 98th percentile 24-hour average PM2.5 concentrations (μg/m3)

Source: Fitz-Simons et al. (2000)

1   1998). Data collected in this study from 1994 to 1998 at all sites show decreases in $PM_{2.5}$ ranging

2   from 2% at Santa Maria to 37% at San Dimas/Glendora.

3   The IMPROVE monitoring network, which consists of sites located primarily in national

4   parks and wilderness areas throughout the U.S., provides $PM_{2.5}$ trends for generally rural areas.

5   Figures 2-7a and 2-7b show the 10 year trend from 1989-1998 at 10 eastern and 24 western

6   IMPROVE sites.[10] At the eastern sites, measured $PM_{2.5}$ decreased about 9 percent from 1992 to

7   1995, but increased about 12 percent from 1995 to 1998. At the western sites $PM_{2.5}$ decreased 11

8   percent from 1989 to 1998. The trend for a single urban IMPROVE site located in Washington,

9   D.C. is shown in Figure 2-7c. At that site, $PM_{2.5}$ concentrations increased about 26 percent from

10   1990 to 1993, then decreased about 23 percent from 1993 to 1995. The 1997 concentration was

11   about 5 percent lower than the 1989 level.

12   As discussed in Section 2.2.4, fine-mode particles are likely to be more uniformly

13   dispersed at urban scales than coarse-mode particles. Analyses of 1999 $PM_{2.5}$ FRM monitoring

14   data from four large metropolitan areas indicate that multiple sites in these urban areas were

15   highly correlated throughout the year. More than 75 percent of the between-site correlation

16   coefficients in Atlanta, Detroit, Phoenix, and Seattle were greater than 0.85 (CD, p. 3-29). In

17   separate studies, similar results were found in Philadelphia during the summers of 1993 and 1994

18   (CD, p. 3-28).

19

20   **2.4.3 $PM_{10-2.5}$**

21       $PM_{10-2.5}$ is a measure of the coarse-mode fraction of PM_{10}, and can be measured by a

22   dichotomous sampler, or by using a difference method with collocated monitors under the same

23   sampling protocol. A nationwide network of samplers using these methods is not available.

24   However, an approximation of $PM_{10-2.5}$ can be made using a difference method on same-day data

25   collected in 1999 from PM_{10} and $PM_{2.5}$ FRM monitors in the same physical location. Since the

26   protocol for each monitor is not identical, the results should be viewed with caution. A more

27   complete and accurate view of $PM_{10-2.5}$ values can be obtained by nationwide deployment of

---

[10] The lines on these figures showing the trend in PM components is discussed in Section 2.4.5.

Concentration, ug/m3
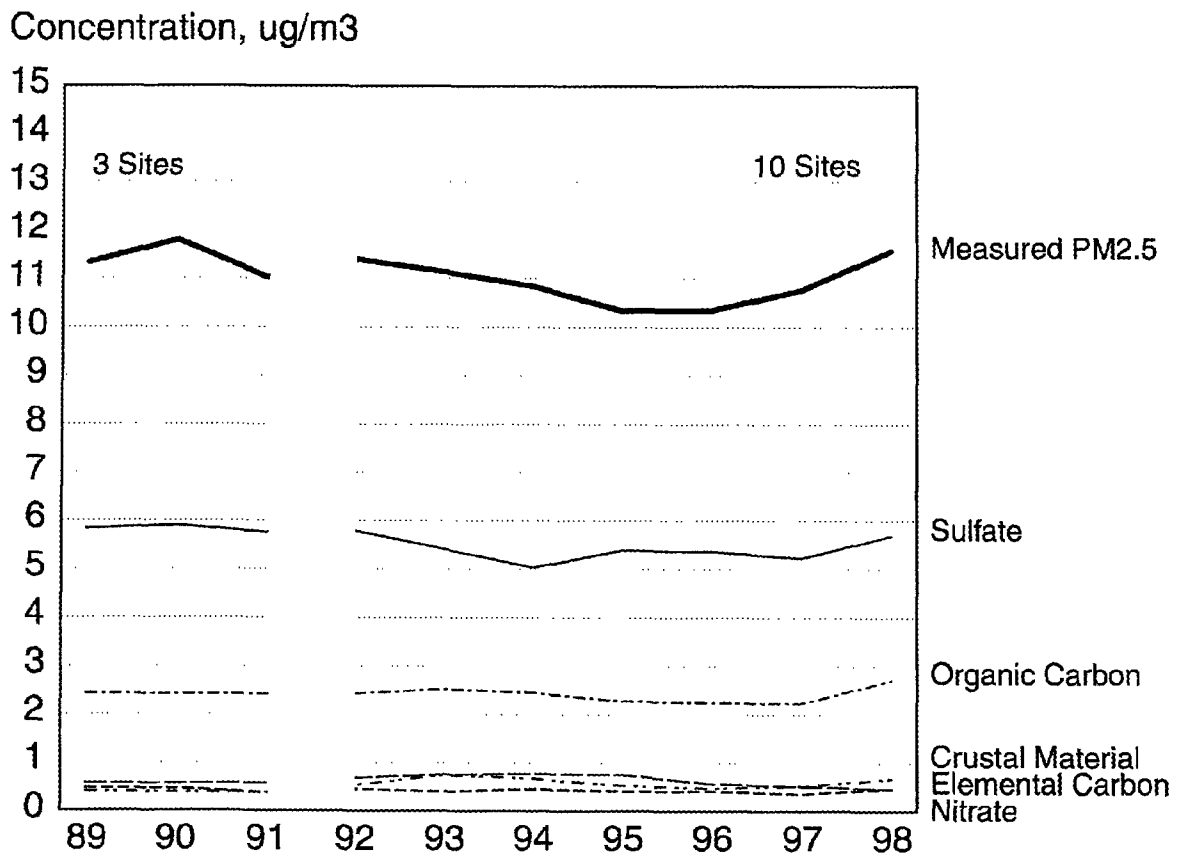
Figure 2-7a. PM$_{2.5}$ Concentrations, 1989-1998 at eastern IMPROVE sites

Source: U.S. Environmental Protection Agency (2000b)

Concentration, ug/m3
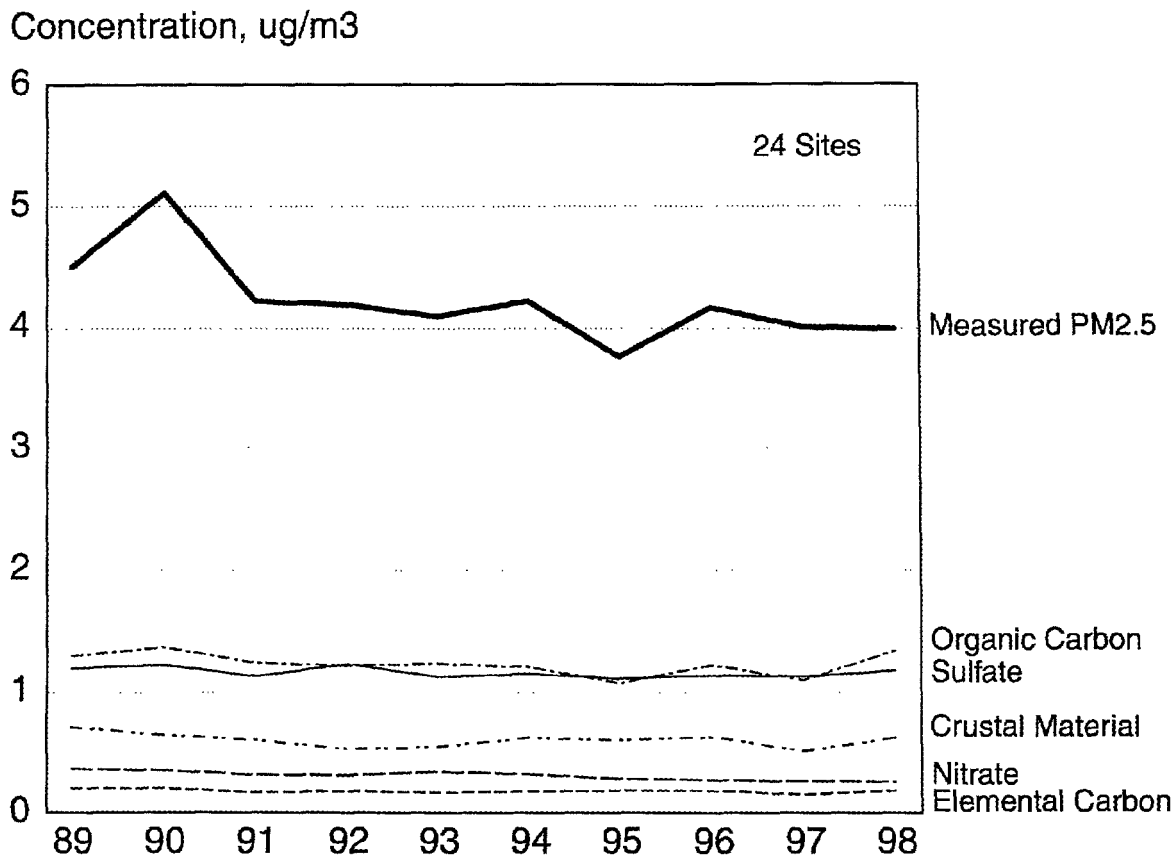
Figure 2-7b. PM$_{2.5}$ Concentrations, 1989-1998 at western IMPROVE sites

Source: U.S. Environmental Protection Agency, (2000b)

Concentration, ug/m3
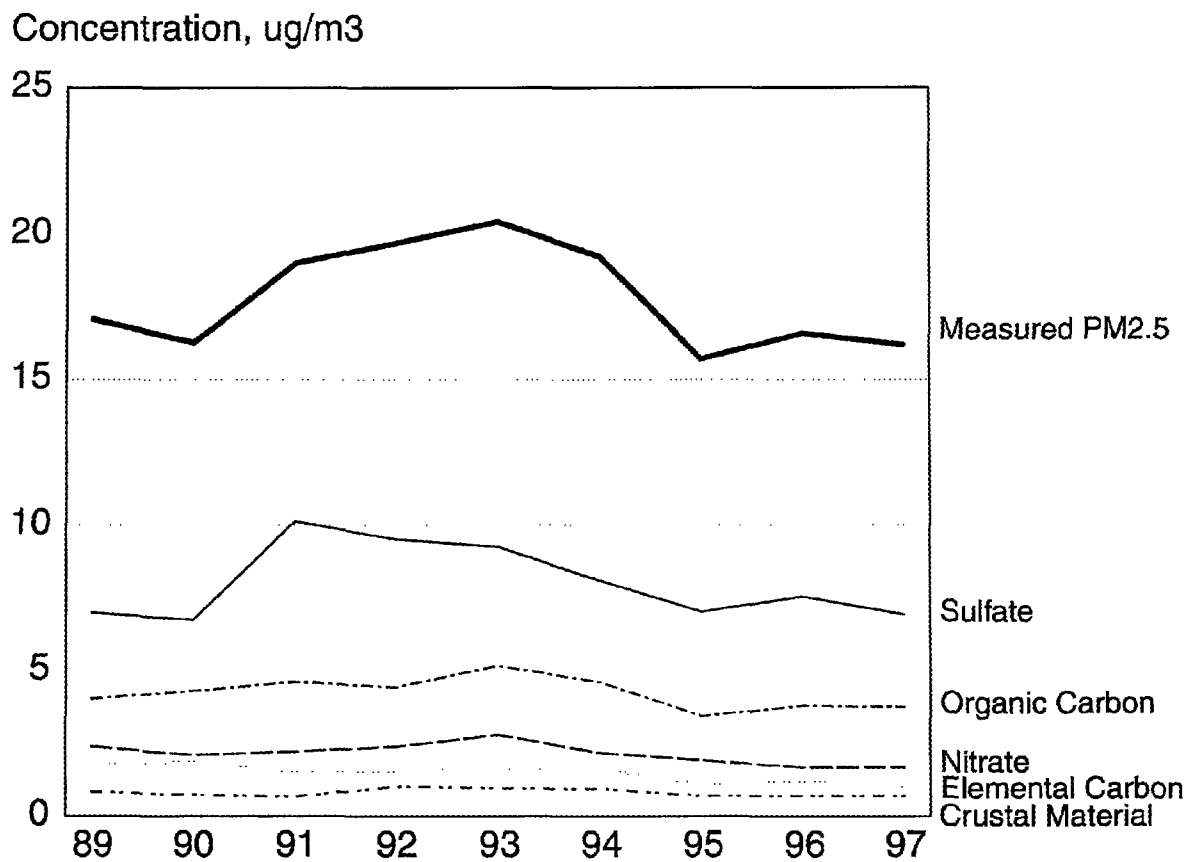
Figure 2-7c. PM$_{2.5}$ Concentrations, 1989-1997 at the Washington, D.C. IMPROVE site

Source: U.S. Environmental Protection Agency (2000b)

1   collocated PM_{10} and $PM_{2.5}$ monitors that use an equivalent monitoring protocol.

2   Figure 2-8a shows estimated annual mean $PM_{10-2.5}$ and Figure 2-8b shows the estimated

3   98th percentile 24-hour average $PM_{10-2.5}$ developed from 1999 FRM monitor data. Since there are

4   currently no data completeness requirements for $PM_{10-2.5}$, the completeness criteria shown in these

5   figures was chosen simply to be consistent with the previous PM_{10} and $PM_{2.5}$ maps. Similarly,

6   since there is no standard for $PM_{10-2.5}$, the annual mean and 98th percentile 24-hour average values

7   were chosen for consistency with the $PM_{2.5}$ maps. The limited data show that annual mean

8   concentrations vary widely, with higher concentrations in several areas of the midwestern U.S.

9   and southern California. A similar pattern emerges for the estimated 98th percentile 24-hour

10   average $PM_{10-2.5}$ concentrations. The southeastern U.S. data are relatively incomplete, but

11   preliminary estimates suggest relatively low $PM_{10-2.5}$ levels throughout that region.

12

13   **2.4.4   Ultrafine Particles**

14   There are no nationwide monitoring networks for ultrafine particles (< 0.1 μm), and only a

15   few recent published studies of ultrafine particle counts in the U.S. At an urban site in Atlanta,

16   Georgia, particles in three size classes were measured on a continuous basis between August 1998

17   and August 1999. The classes included ultrafine particles in two size ranges, 0.003 to 0.01 μm

18   and 0.01 to 0.1 μm, and a subset of accumulation-mode particles in the range of 0.1 to 2 μm

19   (Woo et al., 2000). Figure 2-9 shows the annual average number and volume concentrations for

20   these three size classes. The vast majority, 89%, of the number of particles were in the ultrafine

21   mode (smaller than 0.1 μm), but 83% of the particle volume was in the subset of accumulation-

22   mode particles. The researchers found that for particles up to 2 μm there was little evidence of

23   any correlation between number concentration and either volume or surface area. This suggests

24   that fine-mode particle mass, which arises primarily from particles larger than ultrafines, does not

25   correlate well with particle number, which is dominated by particles in the ultrafine mode.
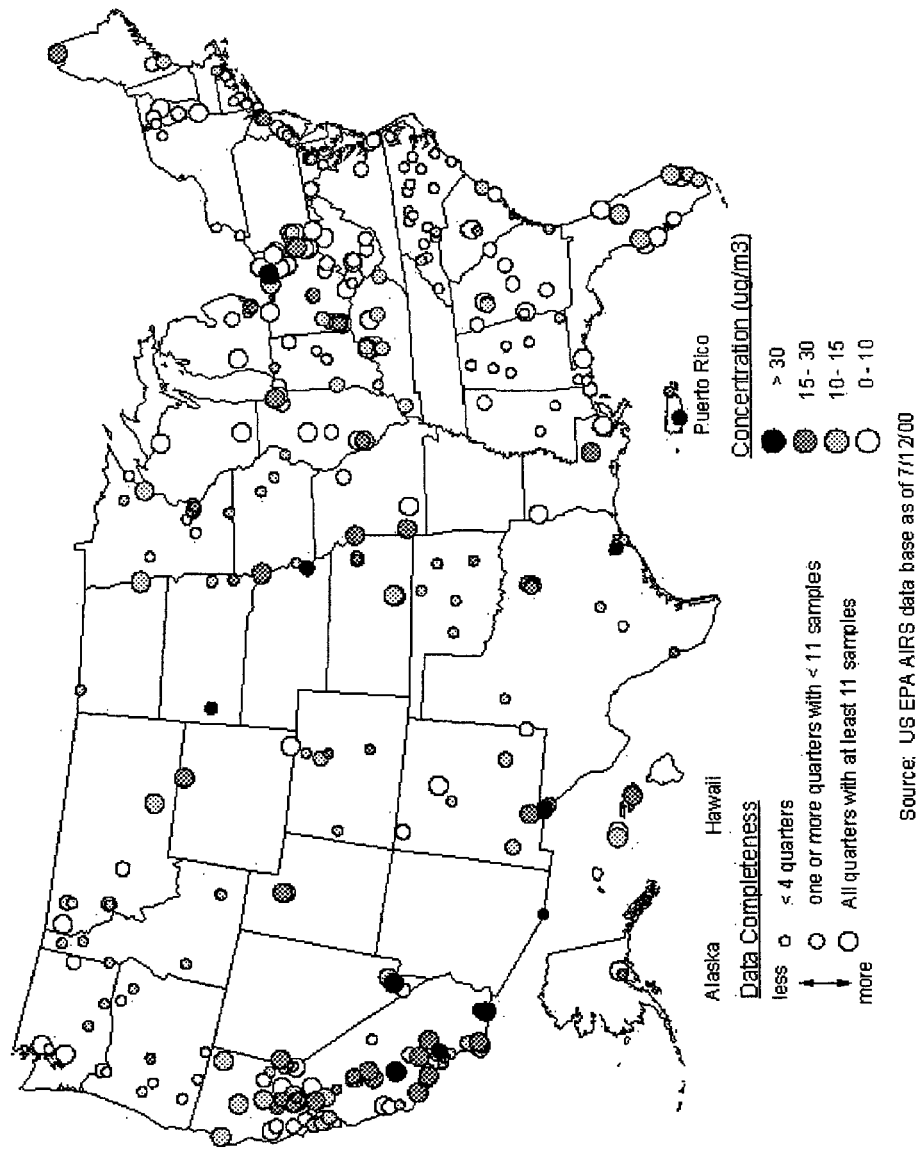
Figure 2-8a. 1999 estimated annual mean PM$_{10-2.5}$ concentrations (μg/m^3)

Source: Fitz-Simons et al. (2000)
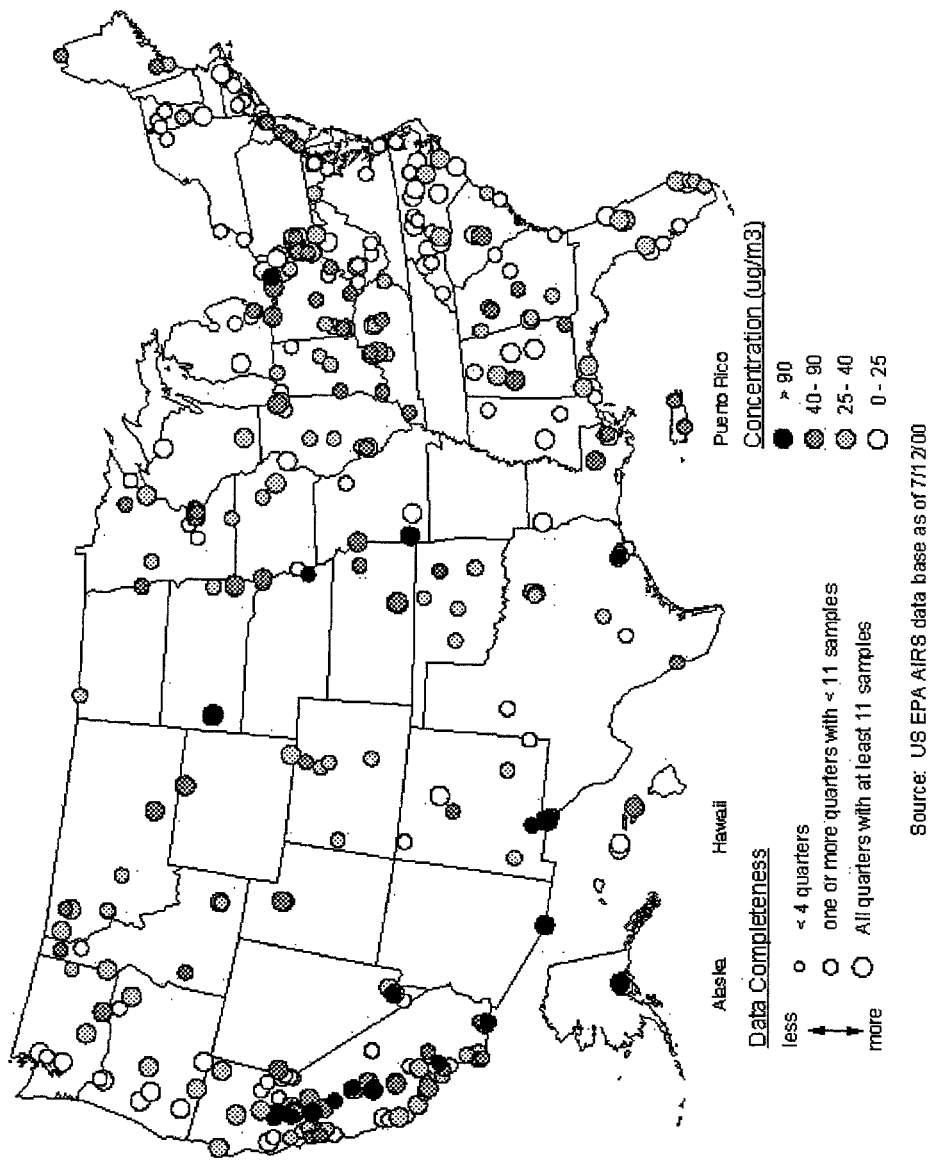
Figure 2-8b. 1999 estimated 98th percentile 24-hour average PM$_{10-2.5}$ concentrations (µg/m^3)

Note: The circle sizes on this map indicating the relative number of data points used to generate the estimates are not entirely accurate. The values, however, are accurate. A new map with revised completeness indicators is being generated.

Source: Fitz-Simons et al. (2000)

Source: US EPA AIRS data base as of 7/12/00

Puerto Rico

Concentration (ug/m3)

● > 90

◉ 40 - 90

◉ 25 - 40

○ 0 - 25

Alaska   Hawaii

Data Completeness

less   ○ < 4 quarters

→   ○ one or more quarters with < 11 samples

more   ○ All quarters with at least 11 samples
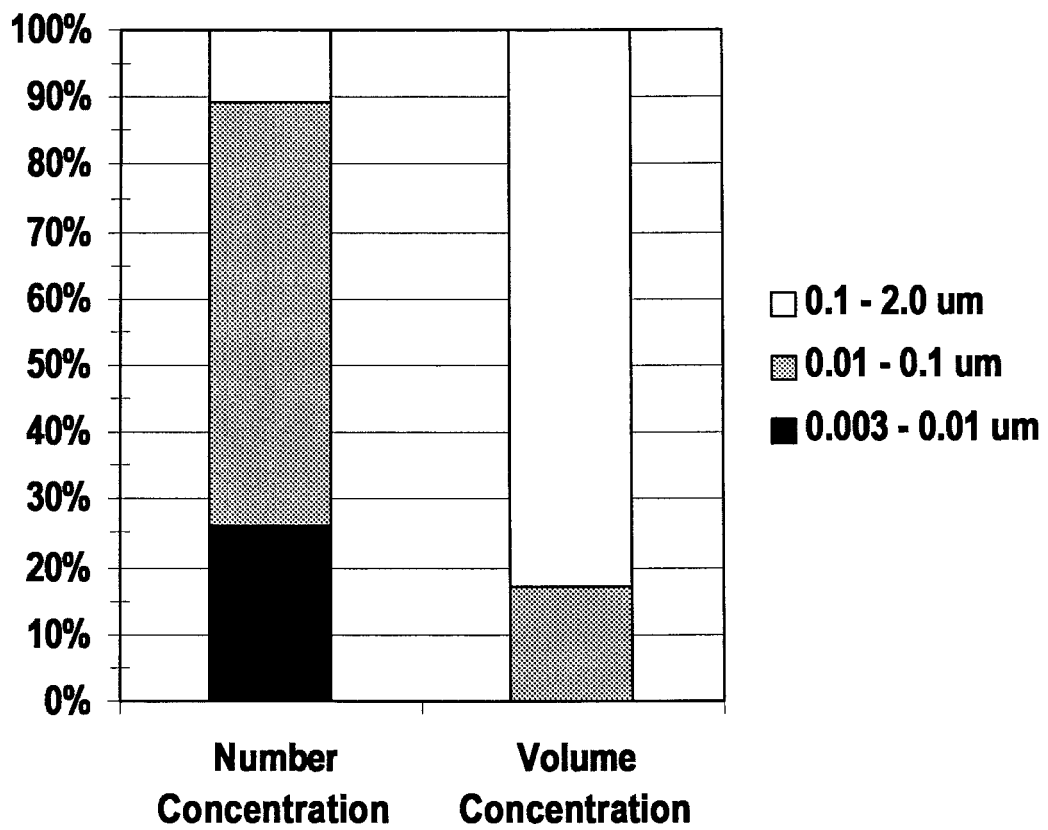
Figure 2-9. Yearly average fractions of fine (0.1–2.0 μm) and ultrafine (0.003–0.01 μm) particle number and volume concentrations in Atlanta

1 ### 2.4.5 Components of PM

2   Atmospheric PM contains many different chemical components that vary by location, time

3 of day, and time of year. The 1996 CD and Staff Paper provided indications of regional

4 composition differences based on data from short-term urban studies and the predominantly rural

5 IMPROVE network. More recent data appears consistent with earlier findings. Table 2-3 shows

6 typical annual average fine fraction mass apportionment among chemical components in the

7 eastern and western U.S. In general, eastern U.S. fine-mode particles are dominated by sulfate,

8 and to a lesser extent by organic carbon. Western U.S. fine-mode particles appear to have a

9 greater proportion of organic carbon, nitrate, and crustal material.

10
11 **Table 2-3. Gross Annual Average Chemical Composition of PM$_{2.5}$ Particles Obtained**
12 **in Rural Areas of the Eastern and Western U.S. by the IMPROVE Network and**
13 **in Mixed Rural, Suburban, and Urban Areas Obtained by Studies Summarized**
14 **in the 1996 PM Criteria Document**

	IMPROVE		1996 PM AQCD	
	Eastern US	Western US	Eastern US	Western US
	% Contribution		% Contribution [a]	
SO$_4^-$	56	33	44	11
EC	5	6	5	14
OC	27	36	27	38
NO$_3$	5	8	1	15
Crustal	7	17	6	14
	Reconstructed PM$_{2.5}$ Concentration (μg/m^3)		PM$_{2.5}$ Concentration (μg/m^3)	
PM$_{2.5}$	11.0	3.9	31.0	37.3

25 [a] Note that contributions do not add to 100% due because a portion of the measured total mass was not
26 chemically characterized.
27 Sources: IMPROVE network – EPA (2000a), 1996 PM Criteria Document – EPA (1996a)

28
29   Trends in remote area concentrations of PM components, generated with data from the

30 IMPROVE network, are shown in Figures 2-7a and 2-7b. All of the components have shown

31 variability of less than 1 μg/m^3 over the ten year period from 1989 to 1998. At the eastern sites

32 sulfate appeared to be declining until 1994, but has risen again in recent years. In 1998 organic

1   carbon was at its highest level over the 10 year period.[11] Data from the urban IMPROVE site in

2   Washington, D.C., shown in Figure 2-7c, indicates that all the components were lower in 1997

3   than at the their peaks during the preceding 8 years. In 1997 sulfate is about 3 $\mu g/m^3$ lower than

4   its 1991 peak of just over 10 $\mu g/m^3$.

5   Data collected from 1994 to 1998 as part of a children's health study in twelve communities

6   in southern California also indicate decreases in major identified components such as nitrate,

7   sulfate, ammonium, and acids (Taylor et al., 1998). However, the undefined components

8   indicated a mixed pattern of increases and decreases at the same sites. A similar downward trend

9   was observed from 1978 to 1995 in nitrate and sulfate concentrations at sites in North Long

10   Beach and Riverside, California (Dolislager and Motallebi, 1999).

11

12   **2.4.6 Relationships Among $PM_{2.5}$, PM_{10}, and $PM_{10-2.5}$**

13   In this section, new information from the nationwide $PM_{2.5}$ FRM monitoring network on the

14   relationship among PM indicators in different regions is presented. Figure 2-10 shows the

15   distribution of 1999 ratios of $PM_{2.5}$ to PM_{10} at sites in different geographic regions. The ratios are

16   highest in the eastern U.S. regions with median ratios from 0.64 to 0.69, and lowest in the

17   Southwest region, with a median ratio of 0.39. These data appear to be generally consistent with

18   earlier findings from a more limited set of sites reported in the 1996 CD.

19   Correlations among pollutant indicators can provide insights into how well one indicator can

20   represent the variability in another indicator. For instance, in some areas PM_{10} may serve as a

21   good indicator of $PM_{2.5}$. Figure 2-11 shows the results of a nationwide analysis of the urban area

22   correlations among PM size fractions using 1999 24-hour average data from the FRM monitoring

23   networks. PM_{10} and $PM_{2.5}$ measured on the same days at collocated sites are fairly well correlated

24   in most parts of the country with the lowest correlations in the Upper Midwest and Southwest.

25   As might be expected from their differences in origin, composition, and behavior, fine-fraction

26   mass ($PM_{2.5}$) is generally not well correlated with coarse-fraction mass

---

[11] Unidentified PM components are an important part of total measured PM mass, and affect the year to year variability in the mass trend. For example, in Figure 2-7b, the upward spike in 1990 and the downward spike in 1995 are dominated by changes in the unidentified fraction.
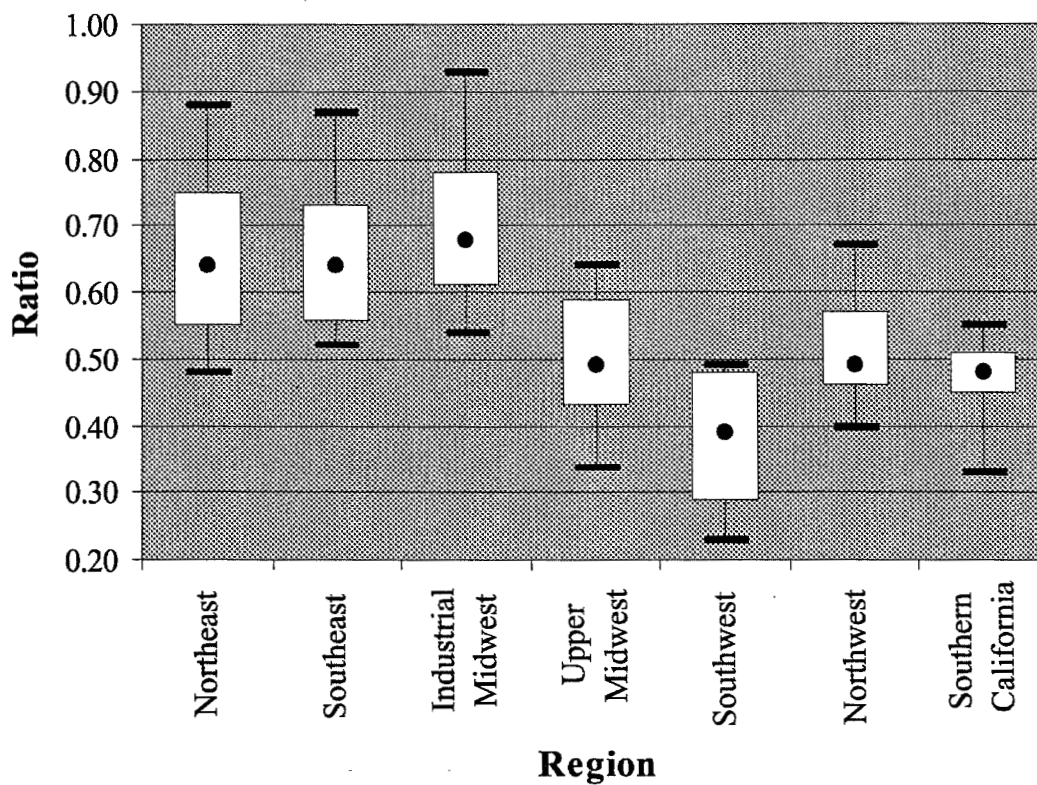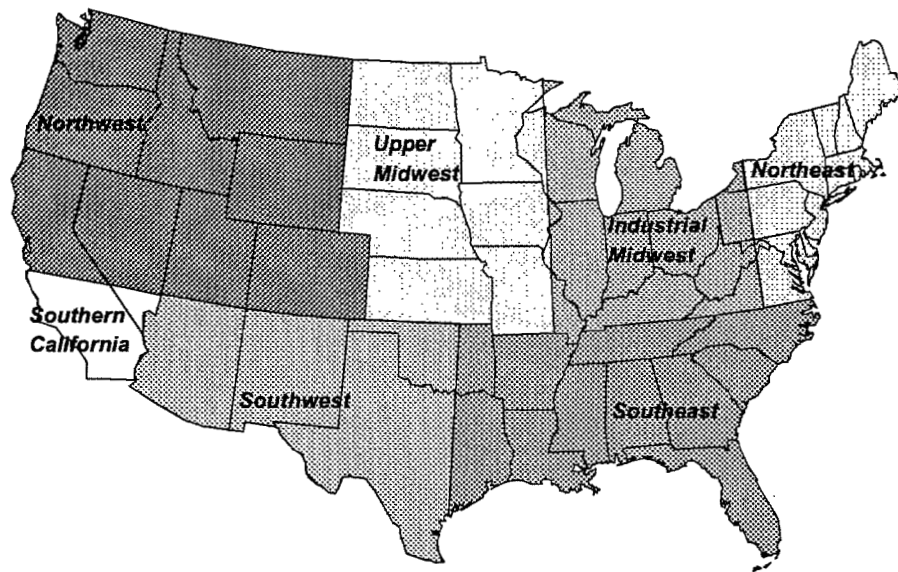
Figure 2-10. Distribution of Ratios of $PM_{2.5}$ to PM_{10} by Region. Box represents upper and lower quartiles of the distribution; whiskers represent 10th and 90th percentiles; black dot represents median.

Source: Adapted from Fitz-Simons et al. (2000), Attachment E
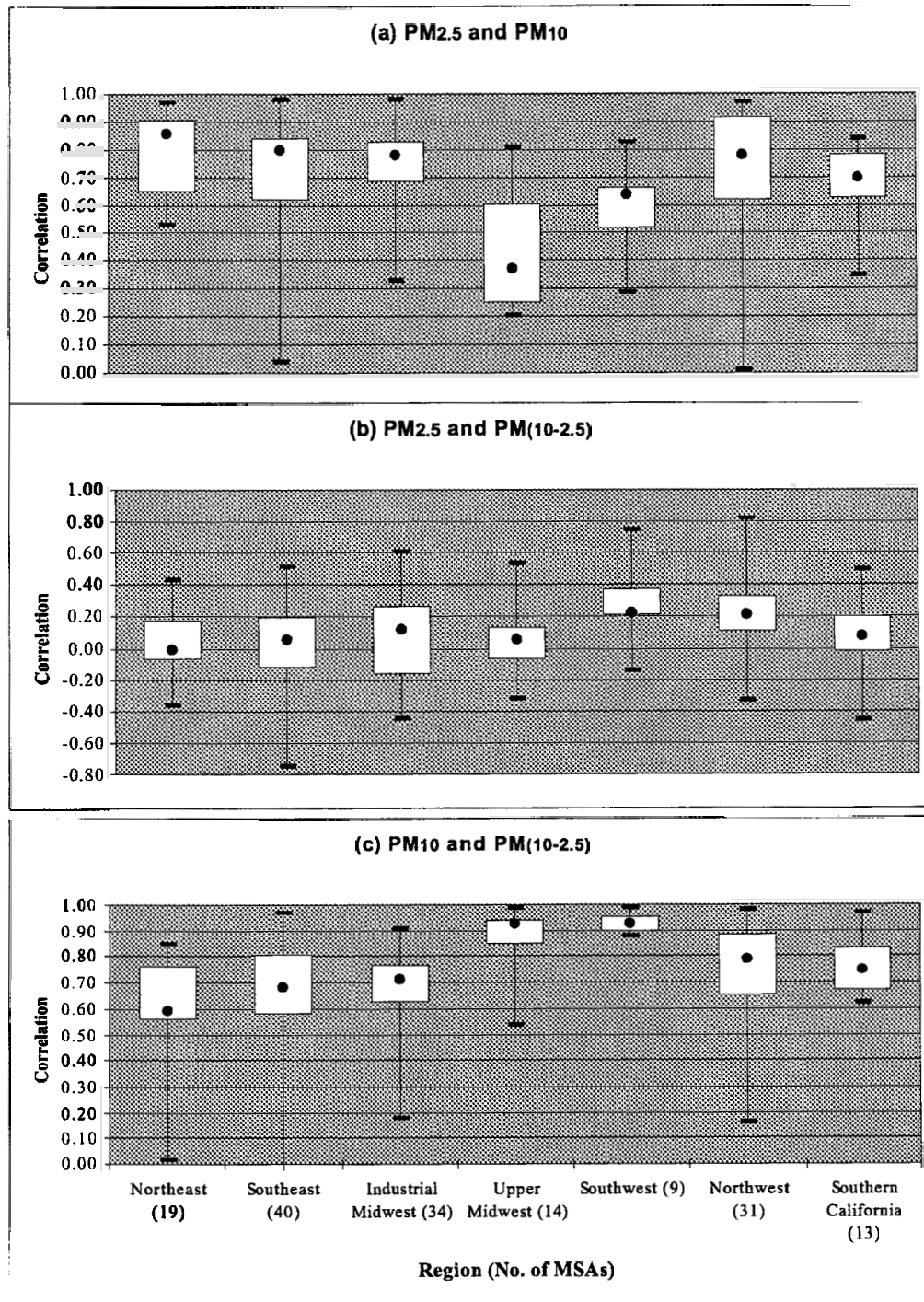
Figure 2-11. Distribution of Urban Area Correlations of 24-hour Average PM by Region. Box represents upper and lower quartiles of the distribution; whiskers represent minimum and maximum; black dot represents median.

Source: Adapted from Fitz-Simons et al. (2000), Attachment 1

1   ($PM_{10-2.5}$). In many cases the correlations are negative. The most consistently high positive

2   correlations of $PM_{2.5}$ to $PM_{10-2.5}$ are in the Southwest, where the low ratio of $PM_{2.5}$ to PM_{10}

3   suggests that crustal material makes a more significant contribution to $PM_{2.5}$ than in other regions.

4   Finally, the correlation between $PM_{10-2.5}$ and PM_{10} is relatively high in all regions, ranging from

5   0.59 in the Northeast to 0.93 in the Upper Midwest and Southwest. The highest correlations

6   appear in regions with low correlations between $PM_{2.5}$ and PM_{10}.

7

8   2.5   TEMPORAL PATTERNS IN PM CONCENTRATIONS

9   2.5.1 $PM_{2.5}$ Patterns

10   Data from the 1999 $PM_{2.5}$ FRM network analyzed by Fitz-Simons, et al. (2000) show

11 distinct seasonal variation in average $PM_{2.5}$ concentrations. Readers should be cautioned that this

12 analysis represents a single year of data, and that patterns may vary from year to year. The

13 summaries in Figure 2-12a (urban) and Figure 2-12b (rural) show the distributions of monthly

14 average concentrations in different geographic regions. The months with peak urban $PM_{2.5}$

15 concentrations vary by region. The urban areas in the eastern regions all show peaks in the

16 summer months (June-August), and the western regions all show peaks in the late fall and winter

17 months (November-January). In most regions the urban and rural patterns are similar, with $PM_{2.5}$

18 concentrations generally lower in rural areas. However, Southern California urban and rural

19 monitors show different seasonal patterns, with urban winter peaks not present in rural areas.

20 Also, in the Northwest the rural winter peak is not as pronounced as it is in urban areas.

21   Using data from a limited number (31) of continuous non-FRM $PM_{2.5}$ monitors, Fitz-Simons

22 et al. (2000) summarized diurnal patterns in $PM_{2.5}$ concentrations. Caution should be used in

23 interpreting data from continuous methods, which can produce significant artifacts related to

24 semi-volatile components (CD, p. 3-22). Figure 2-13 shows the 1999 annual hourly average

25 distribution summary for monitors in each region. In most regions the figure shows a cycle of

26 elevated $PM_{2.5}$ levels between 6:00 a.m. and 9:00 a.m., and again in the evening hours

Figure 2-12a.
1999 Monthly Average Urban PM$_{2.5}$ Distributions by Region. Box represents interquartile range; plus sign is the mean; box line is the median.

Source: Fitz-Simons et al. (2000)
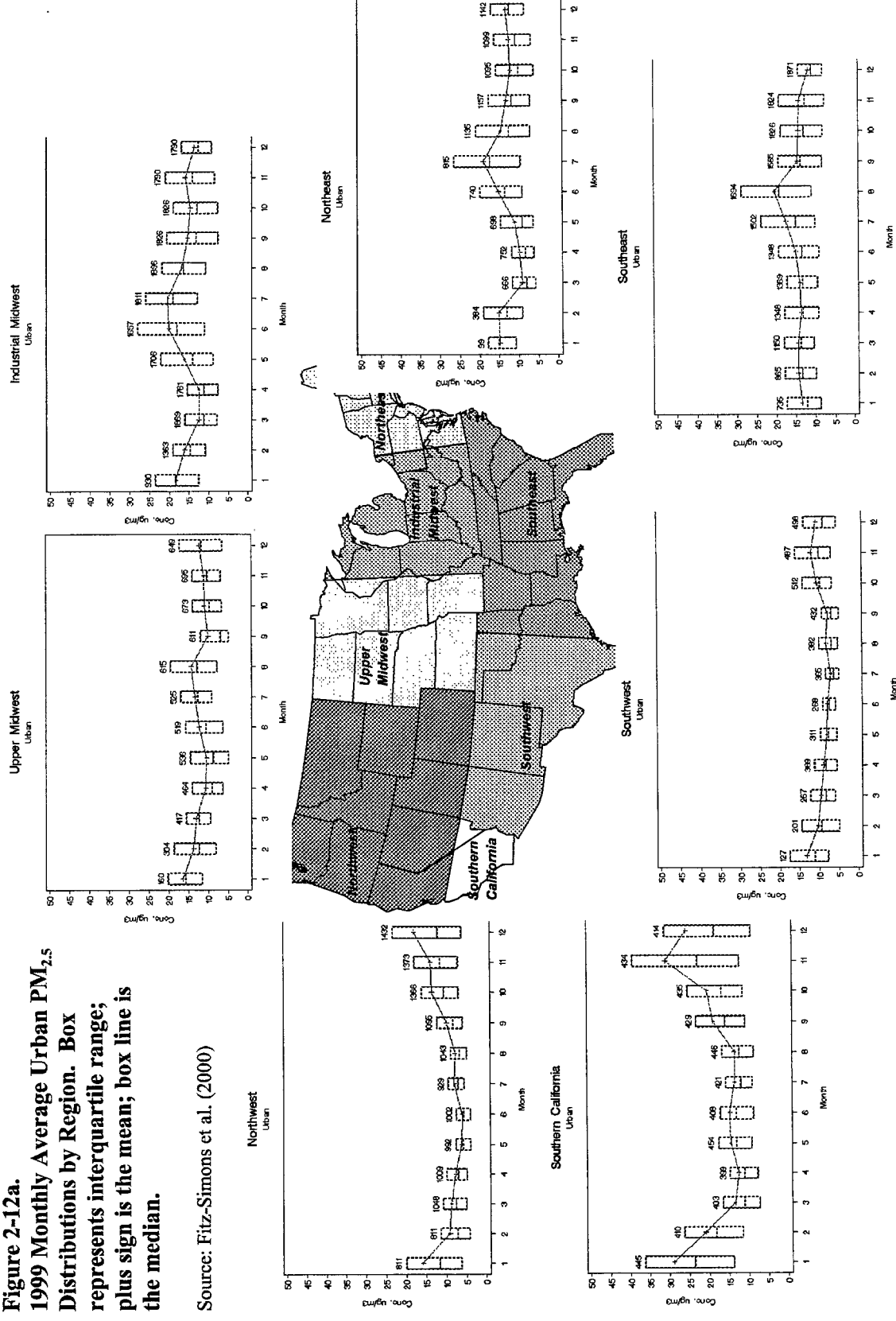
Figure 2-12b.
1999 Monthly Average Rural PM$_{2.5}$ Distributions by Region. Box represents interquartile range; plus sign is the mean; box line is the median.

Source: Fitz-Simons et al. (2000)

June 13, 2001 -- Preliminary Draft
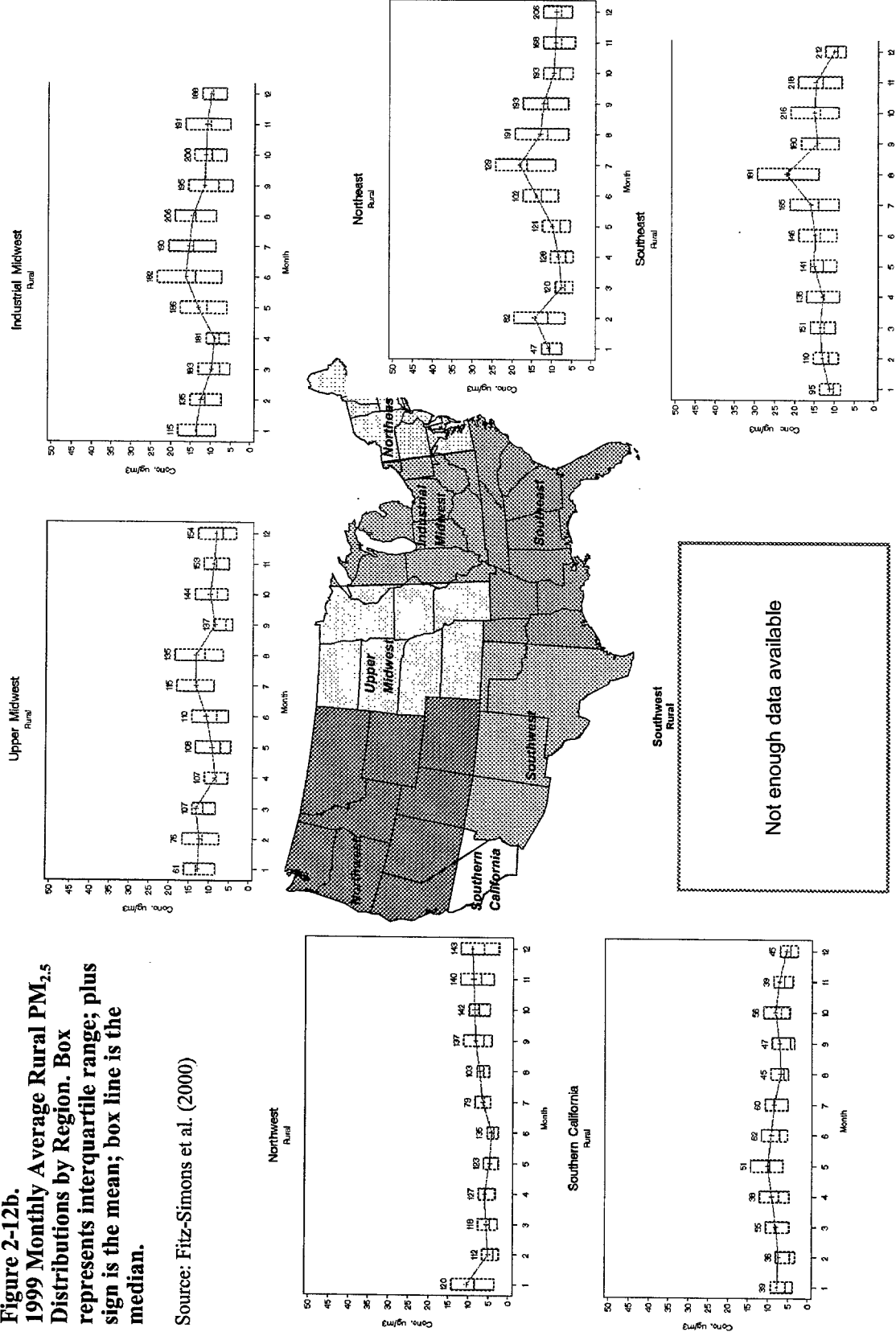
Figure 2-13. 1999 Annual Hourly Average Distribution of PM$_{2.5}$ Concentrations from Continuous Monitors. Box represents interquartile range; plus sign is the mean; box line is the median.
Source: Fitz-Simons et al. (2000)
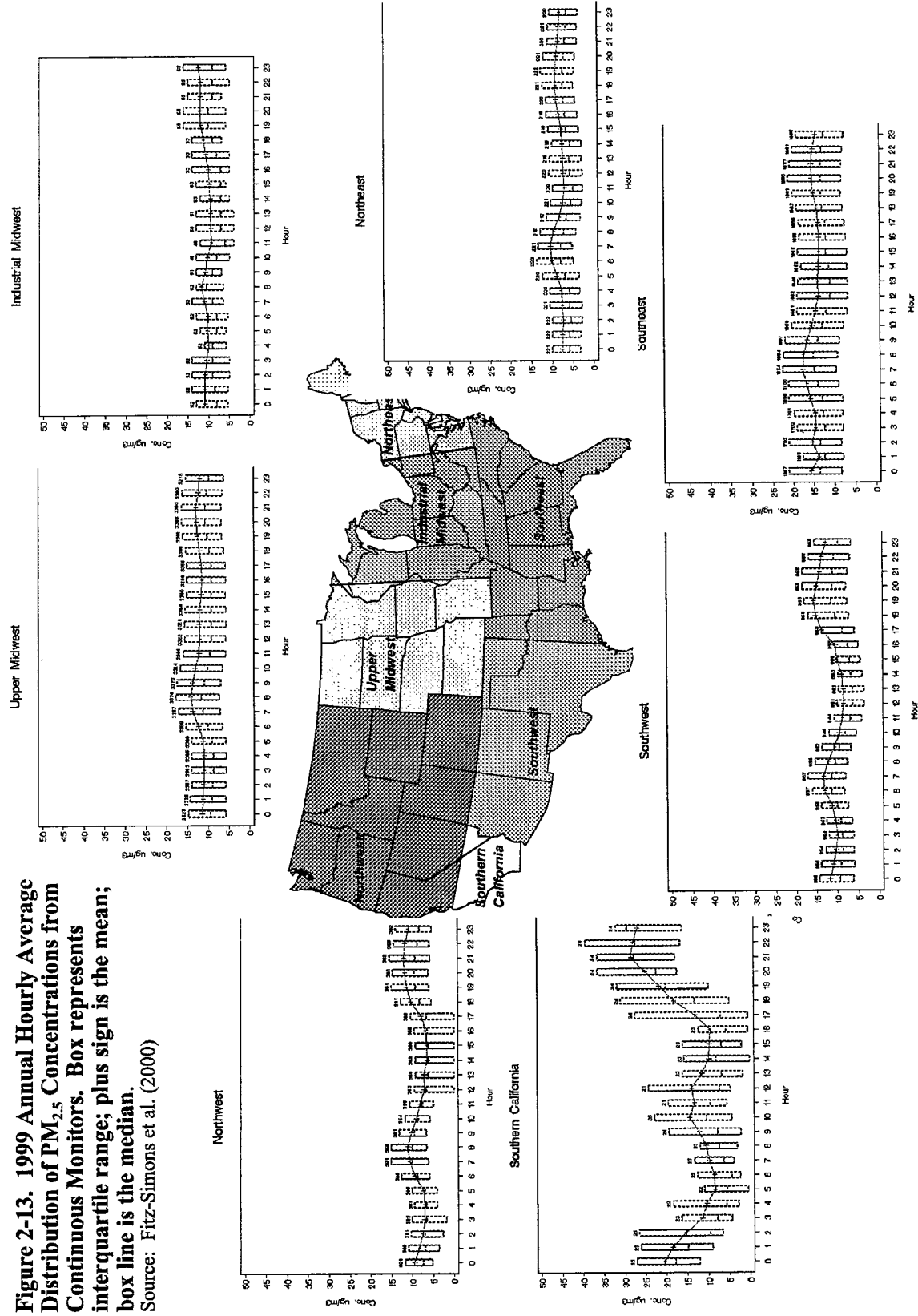
1   starting around 6:00 p.m. However, there is significant variation in day-to-day profiles, as

2   suggested in the box plots by the relatively large ratio of the interquartile range to the median.

3   These cycles vary by location and by calendar quarter, and possibly by the type of monitor and

4   monitor operating procedures.

5   The continuous monitors also provide some insight into short-term (e.g., hourly) increases

6   in $PM_{2.5}$, which might be important to understanding associations between elevated PM levels and

7   adverse health effects. The 1999 data in Figure 2-14 show the distribution of increases from one

8   hour to the next in hourly average $PM_{2.5}$ concentrations. Typical increases (median) range from

9   0.8 $\mu g/m^3$ to 3.0 $\mu g/m^3$, and more atypical increases (95th percentile) range from 4.0 $\mu g/m^3$ to

10   16.4 $\mu g/m^3$. However, rare increases were observed to be an order of magnitude higher than this

11   range.

12

13   **2.5.2 Ultrafine Patterns**

14   Few U.S. studies have extensively examined diurnal or seasonal patterns for ultrafine

15   particles. At an urban site in Atlanta, Georgia, Woo et al. (2000) found that ultrafine particle

16   number concentrations tend to be higher on weekdays than on weekends. Concentrations of

17   particles in the range of 0.01 to 0.1 μm are higher at night than during the daytime, and tend to

18   reach their highest values during morning rush hour. Smaller particles in the range of 0.004 to

19   0.01 μm were elevated during rush hour when temperatures were below 50°F. Several periods of

20   relatively high ultrafine particle levels were observed during the year-long study period from

21   August 1998 to August 1999, and SO_2 measurements show corresponding peaks during these

22   periods.

23

24   **2.6   PM BACKGROUND LEVELS**

25   For the purposes of this document, background PM is defined as the distribution of PM

26   concentrations that would be observed in the U.S. in the absence of anthropogenic, or man-made,

27   emissions of primary PM and precursor emissions of VOC, NO_x, SO_2, and NH_3 in North America.

28   Thus, background includes PM from natural sources and transport of PM from outside of North

29   America. Estimating background concentrations is important for the health risk
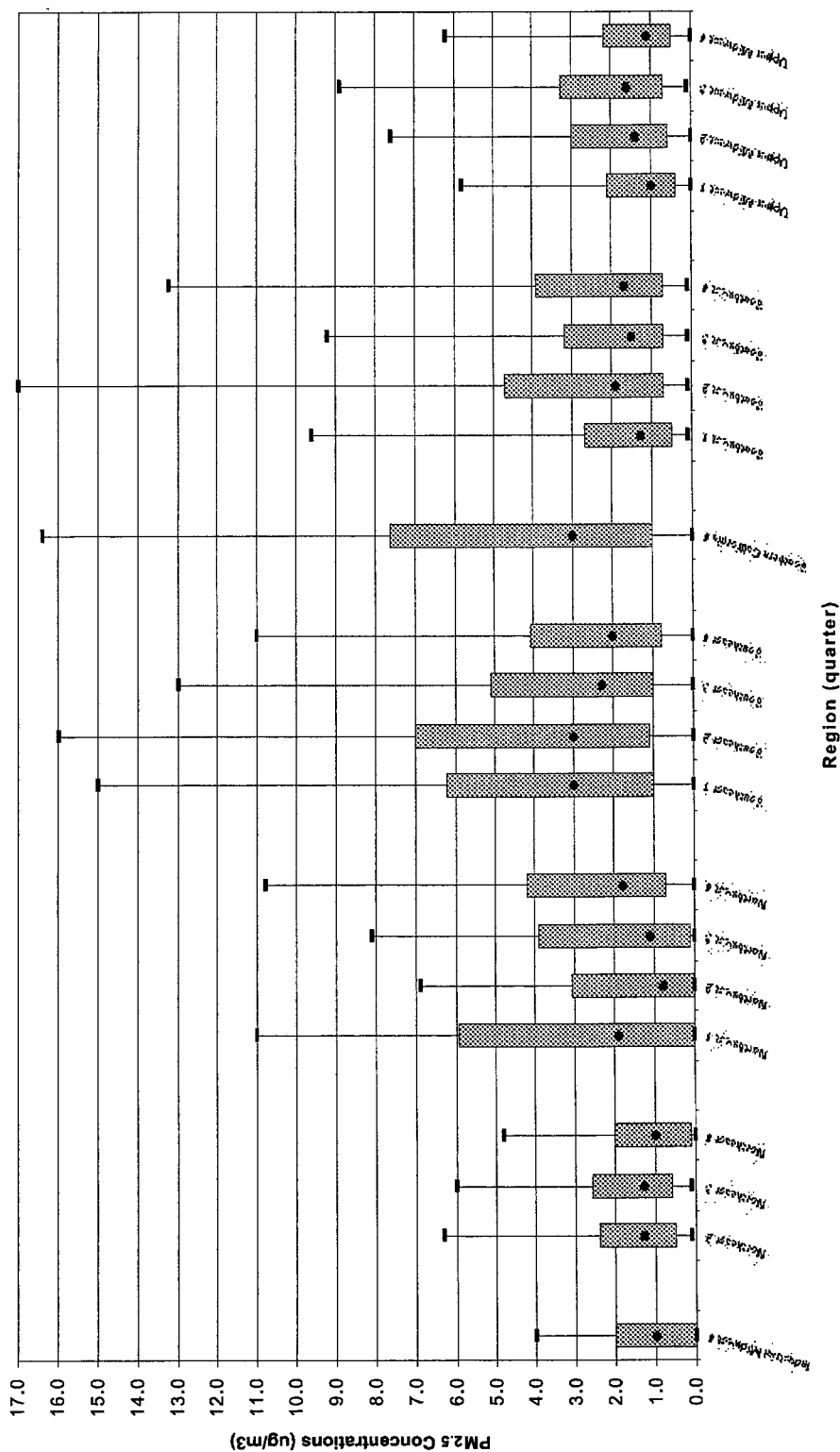
Figure 2-14. 1999 Quarterly Distribution of Hour-to-Hour Increases in Hourly Average PM$_{2.5}$ Concentrations at Continuous Monitors. Bar represents interquartile range; whiskers represent 5th and 95th percentiles; black dot represents the median.

Source: Adapted from Fitz-Simons et al. (2000), Appendix N

1   analyses presented in Chapter 5 and the assessment of ecosystem and visibility effects in Chapter

2   7. The draft CD does not provide any new conclusions about background concentration levels.

3   However, it does discuss the increasing recognition and understanding of the long-range transport

4   of PM from outside the U.S.

5   Background levels of PM vary by geographic location and season, and have a natural

6   component and a human-made (anthropogenic) component. The natural background arises from:

7   (1) physical processes of the atmosphere that entrain small particles (e.g., crustal material, sea salt

8   spray); (2) volcanic eruptions (e.g., sulfates); natural combustion such as wildfires (e.g., elemental

9   and organic carbon, and inorganic and organic PM precursors); and (4) the activities of wild

10   animals and plants (e.g., fine organic aerosols, inorganic and organic PM precursors). The exact

11   magnitude of the natural portion of PM for a given geographic location can not be precisely

12   determined because it is difficult to distinguish local sources of PM from the long-range transport

13   of anthropogenic particles and precursors.

14   PM can be transported long distances from natural events occurring outside the continental

15   United States (CD, p. 3-44). The occurrence and location of these long-range transport events

16   are highly variable and their impacts on the United States are equally variable. Several recent

17   studies have focused on identifying the origin, sources, and impacts of recent transnational

18   transport events.

19   •   The transport of PM from biomass burning in Central America and southern Mexico in 1998

20   has been shown to contribute to elevated PM levels in southern Texas and throughout the

21   entire central and southeastern United States (CD, p. 3-45).

22   •   Wildfires in the boreal forests of northwestern Canada may impact large portions of the

23   eastern United States. Wotowa and Trainer (2000) estimate that a July 1995 Canadian

24   wildfire episode resulted in excess $PM_{2.5}$ concentrations ranging from 5 $\mu g/m^3$ in the

25   Southeast, to nearly 100 $\mu g/m^3$ in the northern Plains States (CD, p. 3-47).

26   •   Windblown dust from dust storms in the North African Sahara desert has been observed in

27   satellite images as plumes crossing the Atlantic Ocean and reaching the southeast coast of

28   the United States, primarily in Florida, and North African dust has also been tracked as far

1 as Illinois and Maine. These events have been estimated to contribute 6 to 11 $\mu g/m^3$ to 24-

2 hour average $PM_{2.5}$ levels during the events in affected areas (CD, p. 3-45).

3 • Dust transport from the deserts of Asia (e.g., Gobi, Taklimakan) across the Pacific Ocean to

4 the northwestern U.S. also occurs. Husar et al. (2000) report that the average PM_{10} level at

5 over 150 reporting stations throughout the northwestern U.S. was 65 $\mu g/m^3$ during an

6 episode in the last week in April 1998, compared to an average of about 20 $\mu g/m^3$ during

7 the rest of April and May (CD, p. 3-45).

8 The draft CD provides the broad estimates of annual average background PM levels shown

9 in Table 2-4. The lower bounds of the ranges are based on compilations of natural versus human-

10 made emissions levels, ambient measurements in remote areas, and regression studies using

11 human-made and/or natural tracers (NAPAP, 1991; Trijonis, 1982). The upper bounds are

12 derived from the multi-year annual averages of the "clean" remote monitoring sites in the

13 IMPROVE network (Malm et al., 1994). Since the IMPROVE data reflect the effects of

14 anthropogenic emissions from within North America, they provide conservative estimates of the

15 upper bounds. There is a definite geographic difference in background levels with lower levels in

16 the western U.S. and higher levels in the eastern U.S. The eastern U.S. is estimated to have more

17 natural organic fine-mode particles and more water associated with hygroscopic fine-mode

18 particles than the western U.S. due to generally higher humidity levels.

19

20 **Table 2-4. Estimated Range of Annual Average PM_{10} and $PM_{2.5}$**

21 **Regional Background Levels**

22

	Western U.S. ($\mu g/m^3$)	Eastern U.S. ($\mu g/m^3$)
PM_{10}	4 - 8	5 - 11
$PM_{2.5}$	1 - 4	2 - 5

25 Source: CD, p. 3-10

26

27 Over shorter periods of time (e.g., days or weeks), the range of expected background

28 concentrations is much broader. Specific natural events such as wildfires, volcanic eruptions, and

1   dust storms can lead to very high levels of PM comparable to, or greater than, those driven by

2   man-made emissions in polluted urban atmospheres.

3

4   **2.7   PM-RELATED SOURCE EMISSIONS AND TRENDS**

5   Insights into what is driving ambient levels of PM can be gained by examining the emissions

6   levels of pollutants that contribute to ambient PM. There is an indirect link between source

7   emissions and ambient concentrations of PM that is affected by complex atmospheric processes,

8   including gaseous chemical reactions and pollution transport.

9   EPA publishes estimates of annual source emissions of pollutants related to ambient criteria

10   pollutant concentrations. The most recent EPA report contains a national inventory of 1998

11   emissions (EPA, 2000a). National emissions estimates are uncertain, and there have been few

12   field studies to test emission inventories observationally. The draft CD concludes that

13   uncertainties in national emissions estimates could be as low as 10 percent for the best

14   characterized source categories (e.g., SO_2 from electric utilities), while emissions estimates from

15   fugitive dust sources should be regarded as order-of-magnitude (CD, p. 3-59). However, recent

16   advances in developing fugitive dust emission factors and emissions algorithms using those

17   factors, and a better understanding of the fate and transport characteristics of fugitive dust

18   emissions released at ground level will reduce the uncertainty of estimates now being developed.

19

20   **2.7.1 Primary PM Emissions**

21   Estimates of directly emitted, or primary, PM are dominated by fugitive dust emissions.

22   Fugitive dust sources include paved and unpaved road dust, dust from construction and

23   agricultural activities, and natural sources like geogenic wind erosion. The majority of directly

24   emitted PM is estimated to be coarse-mode crustal material. Though highly uncertain, estimates

25   of PM_{10} fugitive dust-related emissions are more than 5 times higher than estimates of $PM_{2.5}$

26   fugitive dust-related emissions – 30.9 million short tons compared to 5.5 million short tons (EPA

27   2000a). Recent research has found that about 75 percent of these emissions are within 2 meters

28   of the ground at the point they are measured, and a significant portion are likely to be removed or

29   deposited within a few kilometers of their release point due to turbulence associated with surface

1 topography, or the presence of vegetation or structures (DRI, 2000). This is consistent with the

2 generally small amount of crustal material found in ambient samples in most locations. Estimated

3 annual emissions of directly emitted PM_{10} and $PM_{2.5}$ from the subset of non-fugitive sources in the

4 U.S. are summarized in Figure 2-15. The direct emissions profiles for both $PM_{2.5}$ and PM_{10} are

5 similar, with nearly half of emissions originating from stationary (point and area) source fuel

6 combustion and motor vehicles. A large portion is also attributed to a variety of area source

7 combustion processes, such as open burning. Area source emissions are often more difficult to

8 characterize and are more uncertain than point source emissions.

9 Because total direct emissions of PM are dominated by highly uncertain estimates for

10 fugitive dust sources, the long-term emissions trend for total PM is highly uncertain. Table 2-5

11 shows the 10 year change in primary PM emissions from the subset of non-fugitive dust sources

12 and from all sources. Direct PM_{10} emissions from non-fugitive dust sources were estimated to

13 decline 15 percent from 1990 to 1998 due to reductions from diesel engines, residential wood

14 combustion, and assorted industrial processes, particularly in mineral processing industries. Over

15 the same period primary $PM_{2.5}$ emissions from non-fugitive dust sources were estimated to decline

16 15 percent. However, not all categories of non-fugitive dust sources experienced declines.

17 Emissions of direct $PM_{2.5}$ from coal-based fuel combustion at electric utilities, which comprise

18 nearly 5 percent of the non-fugitive dust total, increased by over 36 percent (EPA 2000a, Table

19 A-6). Due primarily to estimated increases in fugitive dust emissions, primary PM_{10} and $PM_{2.5}$

20 emissions from all sources were estimated to increase by 16 percent and 5 percent respectively.

21

22 **2.7.2 PM Precursor Gas Emissions**

23 Major precursors of secondarily formed fine fraction particles include SO_2, nitrogen oxides

24 (NO_x), which encompasses NO and NO_2, and certain organic compounds. Figures 2-16 and 2-17

25 presents the relative contribution of various sources to nationwide SO_2, NO_x, VOC, and NH_3

26 emissions estimates. Fuel combustion in the electric utility and industrial sectors dominate

27 nationwide estimates of SO_2 emissions. Emissions from motor vehicles make up the greatest

PM₁₀
(3.8 million short tons)

PM₂.₅
(2.9 million short tons)
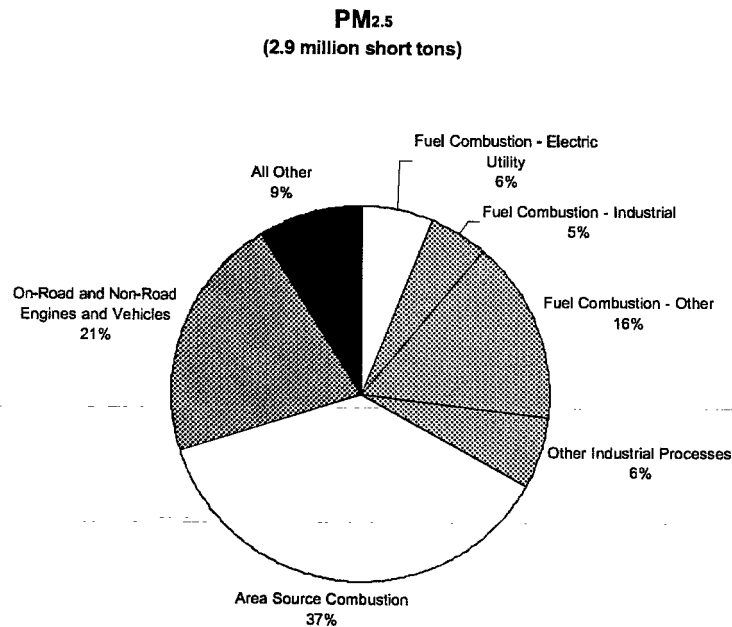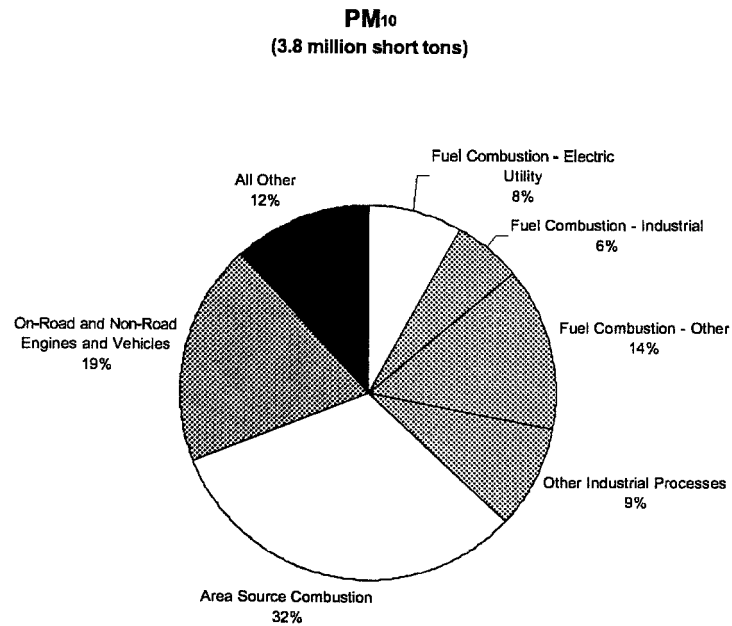
Figure 2-15. 1998 national direct emissions of PM by principal source categories for non-fugitive dust sources

Source: U.S. Environmental Protection Agency (2000a)

Table 2-5. Nationwide Changes in Estimated Annual Emissions of Primary PM and Gaseous Precursors to Secondary PM, 1989 to 1998

	1990 Emissions (million short tons)	1998 Emissions (million short tons)	% Change 1990-1998
Primary PM_{10}			
non-fugitive dust sources	4.5	3.8	-15%
all sources	30.0	34.7	16%
Primary $PM_{2.5}$			
non-fugitive dust sources	3.4	2.9	-15%
all sources	8.0	8.4	5%
SO_2	23.7	19.6	-17%
NO_x	24.0	24.5	2%
VOC	20.9	17.9	-14%
NH_3	4.3	4.9	14%

Source: Environmental Protection Agency (2000a), Tables A-2 through A-8

SO₂
(19.6 million short tons)

On-Road and Non-Road
Engines and Vehicles
7%

All Other
6%

Metals Processing
2%

Fuel Combustion - Other
3%

Fuel Combustion - Industrial
15%

Fuel Combustion - Electric
Utility
67%

NOx
(24.5 million short tons)

All Other
5%

Fuel Combustion - Electric
Utility
25%

On-Road and Non-Road
Engines and Vehicles
53%

Fuel Combustion - Industrial
12%

Fuel Combustion - Other
5%

Metals Processing
0%

Figure 2-16. 1998 nationwide emissions of SO₂ and NOₓ by principal source categories

Source: U.S. Environment Protection Agency (2000a)

VOC
(17.9 million short tons)

All Other
14%

Solvent Utilization
47%

On-Road and Non-Road
Engines and Vehicles
29%

Storage and Transport
10%

Ammonia
(4.9 million short tons)

On-Road and Non-Road
Engines and Vehicles
5%

All Other
4%

Waste Disposal & Recycling
2%

Chemical and Allied Product
Mfg.
3%

Miscellaneous (includes
livestock and fertilizer)
86%
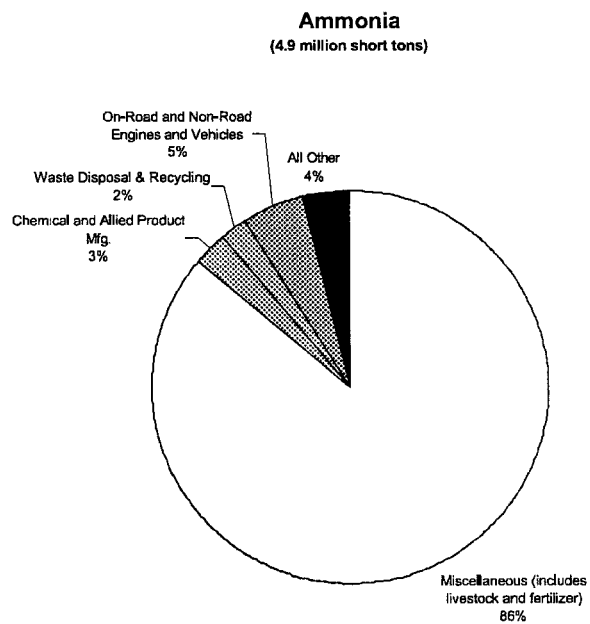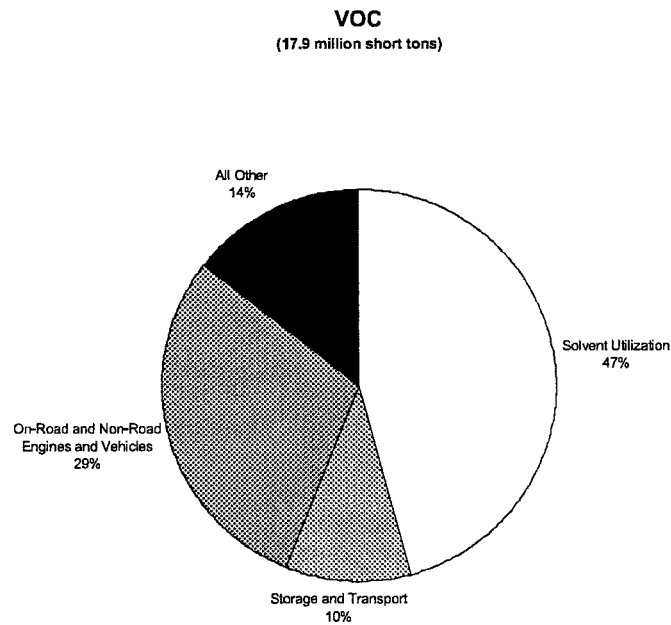
Figure 2-17. 1998 nationwide emissions of VOC and Ammonia by principal source categories
Source: U.S. Environmental Protection Agency (2000a)

1   portion of nationwide NO_x emissions. Motor vehicle emissions also comprise a substantial

2   portion of nationwide VOC emissions, though the greatest contribution comes from the use of

3   various solvents. The vast majority of nationwide NH_3 emissions are estimated to come from

4   livestock operations and fertilizer application, but in urban areas there is a significant contribution

5   from light-duty cars and trucks, as well as certain industrial processes.

6   The relationship between changes in precursor emissions and resulting changes in ambient

7    $PM_{2.5}$ is nonlinear. Thus, it is difficult to project the impact on $PM_{2.5}$ arising from expected

8   changes in PM precursor emissions without air quality simulation models that incorporate

9   treatment of complex chemical transformation processes. While generally SO_2 emissions

10   reductions lead to reductions in sulfate aerosol, and NO_x emissions reductions lead to reductions

11   in nitrate aerosol, the direction and extent of changes will vary by location and season, depending

12   on fluctuations in NH_3 emissions and changes in prevailing meteorology and photochemistry.

13   Table 2-5 shows the 10-year change in estimated national annual PM precursor emissions.

14   Reductions in SO_2 emissions have occurred largely because of CAA programs such as SO_2

15   NAAQS implementation, the Acid Deposition Program, the prevention of significant deterioration

16   (PSD) program, and the new source performance standards (NSPS) program. Despite significant

17   economic growth, NO_x emissions increases have been limited due to PSD, NSPS, the Acid

18   Deposition Program, and mobile source control programs. Future reductions in NO_x are

19   projected for the eastern U.S. from electric utilities as a result of both the Acid Deposition

20   Program and ozone NAAQS implementation. Also, substantial NO_x controls will also be required

21   from motor vehicles in the form of new "Tier 2" standards for light-duty highway vehicles, and

22   new standards for heavy-duty (mostly diesel) highway vehicles. EPA estimates that VOC

23   emissions have declined about 20 percent from 1989 to 1998 due to ozone-related programs and

24   tighter motor vehicle standards. NH_3 emissions were estimated to increase 14 percent due

25   primarily to motor vehicles, fertilizer application and livestock operations.

1 **2.8 RELATIONSHIP BETWEEN HUMAN EXPOSURE TO AMBIENT PM AND**
2 **CENTRAL MONITOR MEASUREMENTS OF PM**

3   The statutory focus of the primary PM NAAQS is on providing protection from adverse

4 effects to public health associated with the presence of PM in the *ambient* air – that is, the focus is

5 on particles that are emitted by sources to the outdoors (i.e., ambient PM). An understanding of

6 human exposure to ambient PM helps inform the evaluation of underlying assumptions and

7 interpretation of results of epidemiological studies that characterize relationships between

8 monitored ambient PM concentrations and observed health effects (discussed in Chapter 3).

9 Further, epidemiological studies of long term exposure raise more complex issues, which are

10 noted in Chapter 3.

11   An important exposure-related issue for this PM NAAQS review is the characterization of

12 the relationships between ambient fixed-site PM concentrations and personal exposure to ambient

13 PM, as characterized by particle size, composition, or other factors. The focus here is on particle

14 size distinctions; the draft CD in Section 5.5 discusses in more detail the exposure relationships

15 related to compositional differences. Information on the type and strength of these relationships,

16 discussed below, is relevant to the evaluation and interpretation of associations found in

17 epidemiological studies using ambient PM concentrations as a surrogate for exposure.[12]

18

19 **2.8.1 Definitions**

20   An individual's exposure to PM results from breathing air containing PM in different types

21 of microenvironments (e.g., outdoors near home, outdoors away from home, indoors at home,

22 indoors at office or school, commuting, restaurants, malls, other public places, etc.) These

23 microenvironments may have different concentrations of PM with particles originating from a

24 wide variety of sources. Exposure is defined as the contact by an individual with a pollutant for a

25 specific duration of time at a visible external boundary (CD, p. 5-1). Average exposure of an

26 individual to PM, averaged over any given time period of length T, can further be expressed as E=

27 $C_i t_i / T$, the sum of the concentration (C_i) of PM in each microenvironment a person spends his or

---

[12] Consideration of exposure measurement error and the effects of exposure misclassification on the interpretation of the epidemiological studies are addressed in Chapter 3.

1   her time in during the course of a day, times the time (t_i) spent in each microenvironment, divided

2   by the total time (T) in all of the microenvironments. Total exposure to an individual is $C_i t_i$, the

3   sum of all exposures during the period T.

4   As discussed in Section 2.7, outdoor concentrations of PM are the result of anthropogenic

5   and natural emissions sources of PM, and are affected by meteorology, atmospheric chemistry,

6   and removal processes. Indoor concentrations of PM are affected by several factors, including

7   ambient outdoor concentrations and processes that result in infiltration of ambient PM into

8   building (e.g., indoor/outdoor air exchange, particle penetration across the building envelope),

9   indoor sources of PM, aerosol dynamics and indoor chemistry, and removal mechanisms such as

10   particle deposition, exfiltration, and air-conditioning and air cleaning devices (CD, p. 5-96).

11   Concentrations of PM inside vehicles are subject to essentially the same factors as indoor

12   concentrations of PM inside the buildings. Total personal exposure to PM has an additional

13   component, the personal cloud, which results specifically from the activities of an individual that

14   typically generate particles affecting only the individual or a small localized area surrounding the

15   person (e.g., walking on a carpet). Personal cloud is assumed to be predominantly due to non-

16   ambient PM sources.

17   In characterizing human exposure to PM concentrations relevant to the NAAQS, the draft

18   CD conceptually separates *total exposure* to PM into exposure to *ambient*[13] PM (*ambient*

19   *exposure*) and exposure to all other sources of PM (*non-ambient exposure*). The draft CD

20   describes PM according to both the source (i.e., ambient or non-ambient) and the

21   microenvironments where the exposure occurs (e.g., outdoors near home, indoors in various

22   rooms, within vehicles). Ambient PM can be differentiated as *ambient-outdoor PM*, outdoor

23   concentrations of ambient PM generally measured at a centrally located fixed site or at specific

24   outdoor locations, including outdoors near home, offices, etc. and *ambient-indoor PM*, ambient

25   PM that has penetrated indoors, entering buildings by infiltration (e.g., through cracks) and bulk

26   flow (e.g., through open windows). *Non-ambient PM* is comprised of PM generated from indoor

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[13] Ambient PM includes not only emissions that are generated outdoors, but also emissions generated indoors and directly vented to the outdoors, such as emissions from wood-stoves, fire places, and some manufacturing processes.

1   sources and the indoor personal cloud. *Indoor-generated* PM is that which is due to indoor

2   sources of particles, which include smoking, cooking, other sources of combustion, cleaning,

3   resuspension, mechanical processes, and chemical reactions. Thus, *indoor PM* is the

4   concentration of PM indoors, and includes ambient-indoor PM, indoor-generated PM, and the

5   personal cloud.

6

7   **2.8.2 Ambient Concentration as a Surrogate for Particle Exposure**

8   The 1996 Criteria Document (EPA, 1996a) presented a thorough review of PM exposure-

9   related studies up to that time. The previous Staff Paper (EPA, 1996b) drew upon the studies,

10 analyses, and conclusions presented in the 1996 Criteria Document and discussed two

11 interconnected PM exposure issues: (1) the ability of central fixed-site PM monitors to represent

12 population exposure to ambient PM, and (2) how differences between fine and coarse mode

13 particles affect population exposures. Distinctions between PM size classes and components were

14 found to be important considerations in addressing representativeness of central monitors. For

15 example, fine-mode particles have a longer residence time and are more uniformly distributed in

16 the atmosphere than coarse-mode particles. The 1996 Staff Paper (EPA, 1996b) concluded that

17 central measurements of daily variations of PM have a plausible linkage to daily variations of

18 human exposures to ambient PM, that this linkage is stronger for fine-mode particles than for

19 coarse-mode or fine-mode plus coarse-mode particles, and within the fine mode stronger for

20 sulfates than for H^+. The 1996 Staff Paper further concluded that "central monitoring can be a

21 useful, if imprecise, index for representing the average exposure of people in a community to PM

22 of outdoor origin." (EPA, 1996b, p. IV-15,16).

23   Exposure studies published since 1996 and reanalyses of studies that appeared in the 1996

24 Criteria Document are reviewed in the draft CD, and provide additional support for the findings

25 made in the 1996 Criteria Document and 1996 Staff Paper. As discussed in the draft CD (CD, p.

26 9-24, 25) and in the discussion that follows, an individual's total personal exposure to PM

27 generally differs from the ambient concentration measured at the central site monitor because of:

28 (1) spatial differences in ambient PM concentrations across a city or region; (2) generally only a

29 fraction of the ambient PM penetrates to indoor or in-vehicle microenvironments; and (3) a

1   variety of indoor sources that produce predominantly ultrafine and coarse-mode particles will

2   contribute to total personal exposure. Thus, the amount of time spent outdoors, indoors, and in

3   vehicles and the types of activities engaged in (e.g., smoking, cooking, vacuuming) also will

4   heavily influence personal exposure to PM.

5   With regard to the first factor that influences the relationship between total personal

6   exposure and concentrations measured at central site monitors, fine-mode particles are more likely

7   to be more uniformly dispersed across urban scales than coarse-mode particles. Analyses of 1999

8    $PM_{2.5}$ FRM monitoring data from four large metropolitan areas indicates that, in general, multiple

9   sites in these urban areas are highly correlated throughout the year, although there are exceptions

10   to this rule (CD, p. 3-57). It is likely that $PM_{2.5}$ concentrations are distributed evenly enough so

11   that one site, or the average of several sites, provides an adequate measure of the community

12   average concentration for $PM_{2.5}$. Where $PM_{2.5}$ is a major fraction of PM_{10} this may also be true

13   for PM_{10}, in other cases, however, there is the potential for large PM_{10} spatial variability in some

14   communities. In some instances the average ambient concentration and the average exposure to

15   ambient PM may differ, but the levels tend to move up and down together. The draft CD

16   acknowledges that this spatial uniformity may not be the case for $PM_{10-2.5}$, for specific chemical

17   components, or for sites located near sources (CD, p. 9-24). At this time there are not sufficient

18   data to assess the spatial variability of ultrafine PM or PM components, except for sulfate, which

19   tends to be regionally uniformly distributed (CD, p. 5-97).

20   The second factor influencing the relationship between ambient PM concentrations and total

21   personal exposure to PM is the extent to which ambient PM penetrates indoors and remains

22   suspended in the air. PM penetration is heavily dependent on the air exchange rate, and also on

23   penetration efficiency and deposition or removal rate, both of which vary with particle

24   aerodynamic size. Air exchange rates (the rates at which the indoor air in a building is replaced by

25   outdoor air) are influenced by building structure, the use of air conditioning and heating, opening

26   and closing of doors and windows, and meteorological factors (e.g., difference in temperature

27   between indoors and outdoors). Based on physical mass-balance considerations, usually the

28   higher the air exchange rate the greater the personal exposure to ambient PM in the indoor and in-

29   vehicle microenvironments. Rates of infiltration of outdoor PM into homes are higher for PM_1

30   and $PM_{2.5}$ than for PM_{10}, $PM_{10-2.5}$, or ultrafine particles (CD, p. 5-97). Since $PM_{10-2.5}$ infiltrates

1   indoors less readily than $PM_{2.5}$ and settles out more rapidly than $PM_{2.5}$, the ambient

2   indoor/outdoor concentration ratios for $PM_{10-2.5}$ are smaller than for $PM_{2.5}$. These considerations

3   suggest that central-site ambient measurements are expected to be more representative of ambient

4     $PM_{2.5}$ personal exposure than ambient PM_{10} or $PM_{10-2.5}$ exposures.

5   The third factor influencing the relationship between ambient concentrations and total

6   personal exposure is the contribution of indoor sources to total personal exposure. Several

7   studies have shown that the contribution of indoor sources to total personal exposure is

8   independent of ambient PM. Indoor PM concentrations are often higher than outdoor

9   concentrations due to the additional PM generated from indoor sources. Indoor sources such as

10   cooking, and smoking generate fine-mode particles, and dusting, vacuuming, and resuspension

11   generate coarse-mode particles. Indoor sources tend to produce coarse-mode and nuclei-mode

12   particles more than accumulation-mode particles (CD, p. 9-25).

13   An important finding is that ambient PM concentrations have been demonstrated to be

14   correlated with ambient exposure but independent of nonambient exposure (CD, p. 5-99). This is

15   illustrated in Figures 2-18a,b,c, which show the empirical relationships between ambient PM_{10}

16   concentrations and (a) total exposure, (b) ambient exposure, and (c) nonambient exposure. The

17   data for these figures are from the PTEAM study[14], which was considered in the previous PM

18   NAAQS review (EPA, 1996a, p. 7-24, 7-88) and has provided more data than any other study for

19   this type of analysis. The regression figures were developed according to models described in

20   Mage et al. (1999) and Wilson et al. (2000) and used parameters estimated by Özkaynak et al.,

21   1996a. Figure 2-18(a) shows the weak relationship between total personal exposure and ambient

22   concentrations. Figure 2-18(b) shows that ambient exposure and ambient concentrations are well

23   correlated (correlation 0.86). Figure 2-18(c) illustrates the independence of nonambient exposure

24   and ambient concentrations and also the high variability of nonambient exposure due to

25   differences found in indoor sources across the study homes.

---

[14] EPA's Particle Total Exposure Assessment Methodology (PTEAM) field study (Clayton et al., 1993; Özkaynak et al., 1996a;b) is one of only two large-scale probability sample based field studies conducted in the U.S. or Canada. The study measured indoor, outdoor, personal PM, the air exchange rate for each home, and time spent in various indoor residential and outdoor microenvironments for 147 subjects/households, 12-hr time periods in Riverside, California.
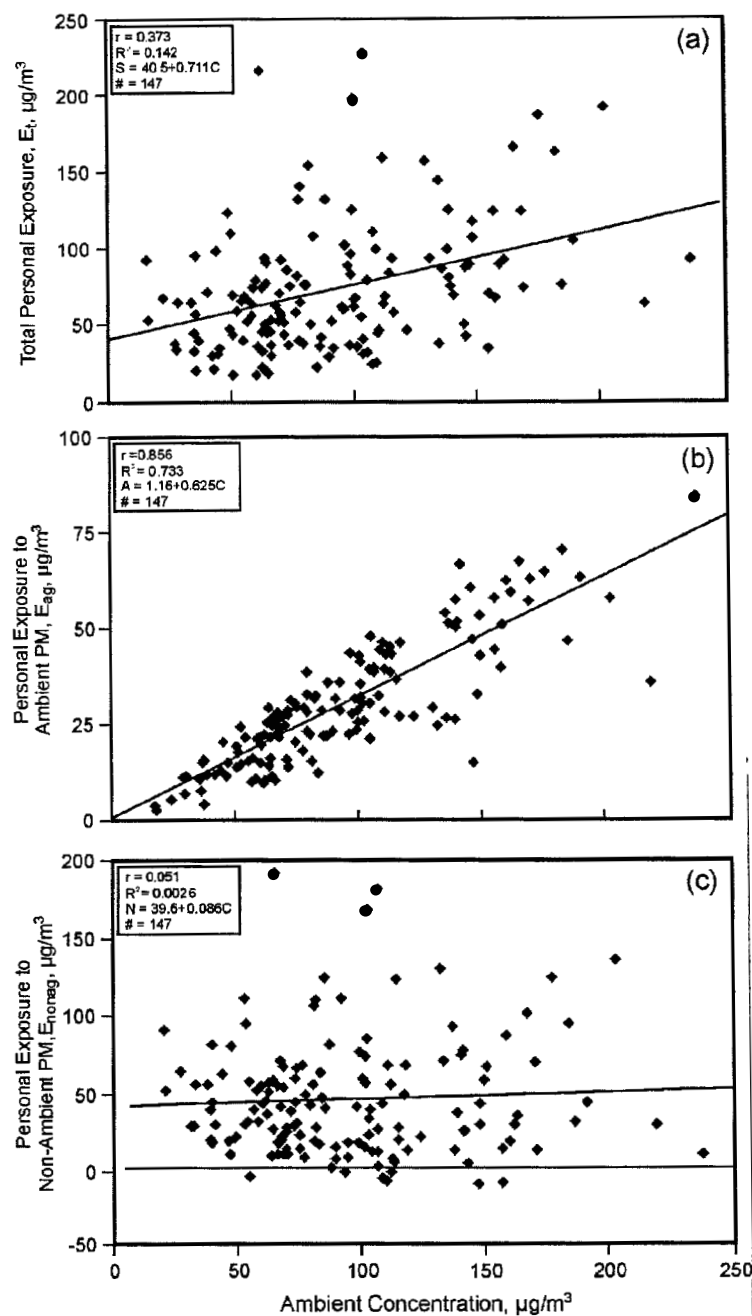
Figure 2-18. Regression analyses of aspects of daytime personal exposure to PM_{10} estimated using data from the PTEAM study. (a) Total personal exposure to PM regressed on ambient concentration, C_a. (b) Personal exposure to ambient PM regressed on C_a. (c) Personal exposure to nonambient PM regressed on C_a.

Source: Draft CD (EPA, 2000a). Data from Clayton et al. (1993).

1   Cross-sectional correlations were reported to be near zero in some exposure studies

2   comparing ambient PM concentrations and total personal exposure to PM across different

3   individuals for the same day. Poor correlations that were found were mainly due to the fact that

4   some subjects lived in homes with low or relatively constant indoor sources and others had many

5   different types of indoor sources. The indoor-generated concentrations are essentially considered

6   a source of random measurement noise on top of the more predictable relationship between

7   ambient PM and exposure to ambient PM. When short-term fluctuations of indoor-generated PM

8   are minimized by taking daily averages and following specific individuals over time (i.e., a

9   longitudinal correlation), the reported correlations between ambient PM and exposure to ambient

10   PM become much stronger. This is probably because the non-ambient contribution for any given

11   individual tends to remain fairly similar over time (e.g., people living with a smoker or using a

12   wood stove in the winter).

13   Furthermore, studies with subjects experiencing small indoor source contributions to their

14   personal exposures (e.g. the elderly in retirement homes), such that total exposure is mostly from

15   ambient PM, generally exhibit both high cross-sectional and high longitudinal correlations

16   between total personal exposure and ambient PM. Correlations between personal and ambient

17   measurements of PM, using a predominantly outdoor component of PM, have shown that indeed

18   the correlations can be quite high when indoor generated PM mass contributions are excluded. In

19   particular, central-site measurements of sulfate (which is primarily fine-mode PM) have also been

20   found to be highly correlated with total personal exposure to sulfate (CD, p. 5-97).

21   The draft CD discusses the finding by some researchers that epidemiology yields statistically

22   significant associations between ambient concentrations and health effects even though there is a

23   near zero correlation between ambient concentrations and [total] personal exposures in many

24   studies (CD, p. 9-85, 86). This has been described by some exposure analysts as an "exposure

25   paradox." The explanation of this seemingly counterintuitive finding is that, as discussed above,

26   total personal exposure includes both ambient and non-ambient generated components. However,

27   community time series epidemiology only addresses the ambient component of exposure. Thus,

28   the appropriate correlation to focus on, for these types of epidemiologic studies, is the correlation

29   between ambient concentration as measured at a central-site monitor or average of several

1	monitors and personal exposure to ambient PM. Also, the appropriate correlation (of ambient

2	concentrations and exposure to ambient PM) is not the pooled correlation of different days and

3	different people, but rather the correlation between daily ambient concentrations and community

4	average daily personal exposure to ambient PM. Based on the review of the available exposure-

5	related studies, the draft CD concludes that for time-series epidemiology, ambient PM

6	concentrations are a useful surrogate for exposure to ambient PM (CD, p. 9-86).

7

8	**2.9 OPTICAL AND RADIATIVE PROPERTIES OF PARTICLES**

9	By scattering and absorbing electromagnetic radiation, ambient particles can impair

10	visibility, affect the amount of ultraviolet radiation that reaches the earth, and affect global climate

11	processes. Electromagnetic radiation is emitted by the sun at ultraviolet (0.015 to 0.4 μm) and

12	visible (0.4 to 0.8 μm) wavelengths, and by the earth at infrared (0.75 to 1000 μm) wavelengths.

13	The effects of ambient particles on the transmission of these segments of the electromagnetic

14	spectrum depend on the radiative properties of the particles, which in turn are dependent on the

15	size and shape of the particles, their composition, the distribution of components within individual

16	particles, and on their vertical and horizontal distribution in the lower atmosphere. In general,

17	radiative effects of particles tend to be at their maximum when the particle radius is similar to the

18	wavelength of the incident radiation (CD, p. 4-129).

19

20	**2.9.1 PM Properties Affecting Visibility**

21	Visibility is affected by scattering and absorption of light in visible wavelengths by particles

22	and gases in the atmosphere (CD, p. 4-88). The efficiency of particles in causing visibility

23	impairment depends on particle size, shape, and composition. Fine-mode particles, especially

24	those in the accumulation mode, are generally most effective in impairing visibility. The fine-

25	mode particle components principally responsible for visibility impairment are sulfates, nitrates,

26	organic matter, elemental carbon, and soil dust. All such particles scatter light to some degree,

27	but only elemental carbon plays a significant role in light absorption. Since elemental carbon,

28	which is a product of incomplete combustion from activities such as the burning of wood or diesel

1   fuel, is a relatively small component of PM in most areas, impairment is generally dominated by

2   scattering rather than absorption.

3   Because humidity causes hygroscopic particles to grow in size, humidity plays a significant

4   role in particle-related impairment. The amount of increase in particle size with increasing relative

5   humidity depends on particle composition (CD, p. 4-91). Humidity-related particle growth is a

6   more important factor in the eastern U.S., where annual average relative humidity levels are 70 to

7   80 percent compared to 50 to 60 percent in the western U.S. Due to relative humidity

8   differences, the same ambient mass concentration of particles would likely cause greater visibility

9   impairment in an eastern location than a western one.

10

11   **2.9.2 PM Properties Affecting Transmission of Ultraviolet Radiation**

12   The transmission of solar radiation in the ultraviolet (UV) range through the earth's

13   atmosphere is affected by ozone, clouds and particles. Of particular interest is the effect of

14   particles on radiation in the ultraviolet-B (UV-B) range (generally from 0.280 to 0.320 μm),

15   which has been associated with various biological effects. Relative to ozone, the effects of

16   ambient particles on the transmission of UV-B radiation are more complex (CD, p. 4-134). The

17   draft CD notes that even the sign of the effect can reverse as the composition of the particle mix

18   in an air mass changes from scattering to absorbing types (e.g., from sulfate to elemental carbon

19   and/or PAH's), and that there is an interaction in the radiative effects of scattering particles and

20   absorbing molecules, such as ozone, in the lower atmosphere.

21   The effects of particles in the lower atmosphere on the transmission of solar UV-B radiation

22   have been examined both by field measurements and by radiative transfer model calculations (CD,

23   pp. 4-134 to 4-137). The draft CD cites several studies that reinforce the idea that particles can

24   play an important role in modulating the attenuation of solar UV-B radiation, although none

25   included measurements of ambient PM concentrations, so that direct relationships between PM

26   levels and UV-B radiation transmission could not be determined. While ambient particles are

27   generally expected to decrease the flux of solar UV-B radiation reaching the surface, any

28   comprehensive assessment of the radiative effects of particles would be location-specific and

29   complicated by the role of particles in photochemical activity in the lower atmosphere. Whether

1   the photochemical production of ozone is enhanced, neutralized, or even reversed by the presence

2   of ambient particles will be location-specific and dependent on particle composition. Also

3   complicating any assessment of solar UV-B radiation penetration to specific areas of the earth's

4   surface are the influences of clouds, which in turn are affected by the presence of ambient

5   particles. The available studies, conducted in diverse locations around the world, demonstrate

6   that relationships between particles and solar UV-B radiation transmission can vary considerably

7   over location, conditions, and time.

8

9   **2.9.3 PM Properties Affecting Climate**

10   The effects of PM on the transfer of radiation in the visible and infrared spectral regions also

11   play a role in global or regional climate. Particles can have both direct and indirect effects on

12   climatic processes. The direct effects are the result of the same physical processes responsible for

13   visibility degradation, namely scattering and absorption (CD, p. 4-152). However, while visibility

14   impairment is caused by particle scattering in all directions, climate effects result mainly from

15   scattering light back toward its source. This reflection of solar radiation back to space decreases

16   the transmission of visible radiation to the surface and results in a decrease in the heating rate of

17   the surface and the lower atmosphere. At the same time, absorption of either incoming solar

18   radiation or outgoing terrestrial radiation by particles, primarily organic carbon, results in an

19   increase in the heating rate of the lower atmosphere.

20   The extent to which ambient particles scatter and absorb radiation is highly dependent on

21   their composition and optical properties and on the wavelength of the radiation. For example,

22   sulfate and nitrate particles effectively scatter solar radiation, and they weakly absorb infrared, but

23   not visible, radiation. The effects of mineral dust particles are complex; they weakly absorb

24   radiation, but their overall effect depends on particle size and reflectivity, and they contribute to

25   atmospheric warming by absorbing infrared radiation. Organic carbon particles mainly reflect

26   radiation, whereas elemental carbon and other black carbon particles (e.g., some PAH's) strongly

27   absorb radiation; however, the optical properties of carbonaceous particles are modified if they

28   become coated with water or sulfuric acid. Upon being deposited onto surfaces, particles can also

1   either absorb or reflect radiation depending in part on the relative reflectivity of the particles and

2   the surfaces on which they are deposited.

3   In addition to these direct effects, particles can also have an indirect effect on climate. For

4   example, sulfate particles can serve as condensation nuclei which alter the size distribution of

5   cloud droplets by producing more droplets with smaller sizes (CD, p. 4-153). Because the total

6   surface area of the cloud droplets is increased, the amount of solar radiation that clouds reflect

7   back to space is increased. Also, smaller cloud droplets have a lower probability of precipitating,

8   causing them to have longer atmospheric lifetimes.

9   The overall radiative effects of particles, both direct and indirect, are not the simple sum of

10   effects caused by individual classes of particles because of interactions between particles and other

11   atmospheric gases. As discussed in Section 4.5.2.2 of the draft CD, the effects of sulfate particles

12   have been the most widely considered, with globally averaged effects of sulfate particles generally

13   estimated to have partially offset the warming effects caused by increases in greenhouse gases.

14   On the other hand, global-scale modeling of mineral dust particles has found that even the sign as

15   well as the magnitude of effects depends on the vertical distribution and effective particle radius.

16   In general, the draft CD makes clear that the effects of PM on climate are complex and not

17   well understood. In general, on a global scale atmospheric particles likely exert an overall net

18   effect of slowing atmospheric warming. However, deviations from global mean values can be

19   very large even on a regional scale, with any estimation of more localized effects introducing even

20   greater complexity. The draft CD concludes that any estimate of the net effect on global climatic

21   processes, and regional or local meteorology and consequent human health or environmental

22   effects, due to location-specific changes in emissions of particles or their precursors would be

23   highly uncertain (CD, p. 4-155).

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3. CHARACTERIZATION OF PM-RELATED HEALTH EFFECTS

1 ## 3.1 INTRODUCTION

2   This chapter summarizes key information relevant to assessment of the known and

3 potential health effects associated with exposure to ambient PM, alone and in combination with

4 other pollutants that are routinely present in ambient air. A comprehensive discussion of this

5 information, focusing on the new scientific information available since the last review, can be

6 found in Chapters 6 - 9 of the draft CD, with Chapter 9 drawing upon the new information to

7 update the integrated assessment provided in the 1996 PM CD.

8   The presentation here organizes the key health effects information into those elements

9 essential for the evaluation of current and alternative standards for PM. Drawing primarily upon

10 the epidemiological, toxicological, dosimetry, and exposure-related information in the draft CD,

11 this chapter summarizes: (1) information and hypotheses regarding mechanisms by which particles

12 that penetrate to and deposit in various regions of the respiratory tract may exert effects; (2) the

13 nature of effects that have been associated with ambient PM, with a focus on fine- and coarse-

14 fraction PM; (3) the identification of sensitive populations that appear to be at greater risk to the

15 effects of ambient PM; and (4) issues related to interpretation and evaluation of the health effects

16 evidence, including discussion of the role of co-pollutants, evidence for effects of various PM

17 components, and issues regarding assessment of epidemiological evidence. Staff conclusions and

18 recommendations related to primary standards for PM will be incorporated into Chapter 6 of a

19 subsequent draft of this Staff Paper.

20   In the last review, a variety of health effects had been associated with ambient PM at

21 concentrations extending from those found in the historic London episodes down to levels below

22 the 1987 PM_{10} standards. Of particular importance from the last review were the conclusions that

23 (1) ambient particles smaller than 10 μm that penetrate into the thoracic region of the respiratory

24 tract remain of greatest concern to health, (2) the fine and coarse fractions of PM_{10} should be

25 considered separately for the purposes of setting ambient air quality standards, and (3) the

26 consistency and coherence of the health effects evidence greatly adds to the strength and

27 plausibility of the observed PM associations. Important uncertainties remained, however, such as

1 issues related to interpreting the role of gaseous co-pollutants in PM associations with health

2 effects, and the lack of accepted biological mechanisms that could explain observed effects.

3 An unprecedented number of new studies containing further evidence of serious health

4 effects have been published since the last review, with important new information coming from

5 epidemiological, toxicological, controlled human exposure, and dosimetry studies. For example,

6 important new epidemiological studies include:

7 • Multi-city studies that use uniform methodologies to investigate the effects of PM on
8   health with data from multiple locations with varying climate and air pollution mixes,
9   contributing to increased understanding of the role of various confounders, including
10   gaseous co-pollutants, on observed PM associations.
11

12 • Several studies evaluating independent associations between effects and fine- and coarse-
13   fraction particles, as well as specific components (e.g., ultrafines, crustal[1] particles).
14

15 • New analyses and approaches to addressing issues related to confounders, possible effects
16   thresholds, and measurement error and exposure misclassification.

17 • Studies presenting new factor analysis methods to evaluate health effects associated with
18   different PM source types.
19

20 Important new toxicological, controlled human exposure, and dosimetry studies include, for

21 example:

22 • Animal and controlled human exposure studies using concentrated ambient particles
23   (CAPs), new indicators of response (e.g., heart rate variability), as well as animal models
24   representing sensitive subpopulations, that are relevant to the plausibility of the
25   epidemiological evidence and provide insights into potential mechanisms for PM-related
26   effects.
27

28 • Dosimetry studies using new modeling methods and controlled exposures that provide
29   increased understanding of the dosimetry of different particle size classes and in members
30   of potentially sensitive subpopulations, such as people with chronic respiratory disease.
31

32 Based on an evaluation of the new evidence and consideration of possible alternative

33 explanations for the reported PM effects, the draft CD concludes that fine- and coarse-fraction

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[1] "Crustal" is used here to describe particles of geologic origin, which can be found in both fine- and coarse-fraction PM.

1   particles should continue to be treated as distinct subclasses of PM (CD, p. 9-1); that "the

2   reported associations of PM exposure and effects are valid;" and that the newer evidence

3   . . . (a) further substantiates associations of such serious health effects with U.S.
4   ambient PM_{10} levels, (b) also more strongly establishes fine particles . . . as likely
5   being important contributors to the observed human health effects, and (c) now
6   provides additional information on associations between coarse-fraction ($PM_{10-2.5}$)
7   particles and adverse health impacts. The overall coherence . . . strengthens the
8   1996 PM AQCD evaluation suggesting a likely causal role of ambient PM in
9   contributing to the reported effects. (CD, p. 9-2)

10

11   **3.2   MECHANISMS**

12   This section briefly summarizes available information concerning the penetration and

13   deposition of particles in the respiratory tract and outlines hypothesized physiological and

14   pathological responses to PM, drawing from information presented in previous PM criteria and

15   standard reviews and in Chapters 7 - 9 of the draft CD. The 1996 staff analysis of this

16   information concluded that the available toxicological and clinical information yields no

17   demonstrated biological mechanism(s) that can explain the associations between ambient PM

18   exposure and mortality and morbidity reported in community epidemiologic studies (EPA, 1996b,

19   p. V-2). While that conclusion still holds true, substantial progress has been made in identifying

20   and understanding a number of potential pathways that were the subject of speculation in the last

21   review. The major purposes of the discussion presented here are to note the available

22   information of greatest relevance in identifying those fractions of PM that are most likely to be of

23   concern to health, to examine possible links between ambient particles deposited in various

24   regions of the respiratory tract and reported effects in humans, to identify factors that may

25   contribute to susceptibility in sensitive populations, and to focus attention on the advances in

26   mechanistic research that are providing evidence in support of a biological basis for a causal link

27   between ambient PM exposures and reported health effects.

28   As discussed in the 1996 Staff Paper, an evaluation of the ways by which inhaled particles

29   might ultimately affect human health must take account of patterns of deposition and clearance in

30   the respiratory tract. The draft CD stresses that the probability of any biological effect of PM

31   depends on particle deposition and retention, as well as underlying dose-response relationships

1   (CD, p. 9-32). The major elements of these considerations have been developed in previous

2   reviews and are summarized briefly here. The human respiratory tract can be divided into three

3   main regions: (1) extra-thoracic, (2) tracheobronchial, and (3) alveolar (CD, p. 9-27). The

4   regions differ markedly in structure, function, size, mechanisms of deposition and removal, and

5   sensitivity or reactivity to deposited particles; overall, the concerns related to ambient particles are

6   greater for the two lower regions (EPA, 1982b; CD, Chapter 7). The junction of conducting and

7   respiratory airways appears to be a key anatomic focus; many inhaled particles of critical size are

8   deposited in the respiratory bronchioles that lie just distal to this junction, and many of the

9   changes characteristic of emphysema involve respiratory bronchioles and alveolar ducts (Hogg et

10   al., 1968). Recent modeling work has documented that ultrafine, as well as larger particles show

11   enhanced deposition of particles at airway bifurcations (Heistracher and Hofmann, 1997;

12   Hofmann et al., 1996). The potential effects of deposited particles are influenced by the speed

13   and nature of removal. These clearance and translocation mechanisms that vary with each of the

14   three regions (CD, Table 7-1, Figure 7-2).

15   Deposition of ambient particles in the three regions of the respiratory tract does not occur

16   at divisions clearly corresponding to the atmospheric aerosol distributions shown above in

17   Chapter 2. The draft CD summarizes simulations of deposition of ambient particle distributions

18   that indicate fine- and coarse-fraction particles are deposited in both the tracheobronchial and

19   alveolar regions (CD, Chapter 7). While fine- ($\leq$2.5 μm) and coarse-fraction (10 - 2.5 μm)

20   particles deposit to about the same extent on a percent particle mass basis in the trachea and

21   upper bronchi, a distinctly higher percent of fine mass (than coarse) deposits in the alveolar

22   region. It follows from the relationships summarized here in Chapter 2 that most of the particle

23   surface area and numbers that deposit are associated with the fine fraction. The draft CD notes

24   that the number dose (particles/cm^2/day) of fine particles to the lung is orders of magnitude higher

25   than that for coarse-fraction particles.

26   Information from the last review, as well as important new studies discussed in the draft

27   CD, add to evidence from the earlier 1987 review, showing how breathing patterns and

28   respiratory disease status can affect regional particle deposition patterns. The 1996 CD showed

29   that as mouth-breathing or workload increases so does deposition in the bronchial and alveolar

1   regions. For those individuals considered to be mouth breathers, deposition increases for coarse-

2   fraction particles in the tracheobronchial region (EPA, 1996a, pp. 166-168). Bennett et al.

3   (1997b) found people with chronic obstructive pulmonary disease (COPD) had about 2.5 times

4   the average deposition rates of healthy adults, related both to elevated tidal volume and breathing

5   rate. In such a case, the respiratory condition can enhance sensitivity to inhaled particles by

6   increasing the delivered dose to sensitive regions. Such dosimetry studies are of obvious

7   relevance to identifying sensitive populations, which is discussed more fully in Section 3.4.

8   As discussed in the 1996 Staff Paper, evidence from epidemiological studies of

9   occupational and historical community exposures and laboratory studies of animal and human

10   responses to simulated ambient particle components suggested that at exposures well above the

11   current PM_{10} standards, particles may produce physiological and ultimately pathological effects by

12   a variety of mechanisms. Previous criteria and standards reviews included an integrated extensive

13   examination of available literature on the potential mechanisms, consequences, and observed

14   responses to particle deposition organized according to major regions of the respiratory tract

15   (EPA, 1982b, 1996a,b). Based on these assessments and considering the composition of typical

16   urban PM, staff concluded, with CASAC concurrence (Friedlander, 1982; Wolff, 1996), that

17   particles that deposit in the thoracic region (tracheobronchial and alveolar regions), i.e. particles

18   smaller than 10 μm diameter, were of greatest concern for standard setting (EPA, 1996b, p. V-3,

19   Figure V-1). Although more recent information has expanded our understanding of these issues,

20   no basis has emerged to change that fundamental conclusion.

21   In the last two reviews, staff identified a number of *potential* mechanisms and supporting

22   observations by which common components of ambient particles that deposit in the thoracic

23   region, alone or in combination with pollutant gases, might produce health effects (EPA, 1982b,

24   Table 5-2; 1996b, Table V-2). While there has been little doubt in the scientific community that

25   the historical London air pollution episodes had profound effects on daily mortality and morbidity,

26   no combination of the mechanisms/observations advanced in the past reviews has been sufficiently

27   tested or generally accepted as explaining the historical community results. Moreover, the

28   potential mechanisms cited in those previous reviews were based on insights developed from

29   laboratory and occupational/community epidemiological studies that involved concentrations that

1   were substantially higher than those observed in current U.S. atmospheres, and in many cases
2   using laboratory-generated particles that may be of limited relevance to community exposures
3   (EPA, 1996b, p V-4).
4   Fully defining the mechanisms of action for PM would involve description of the
5   pathogenesis or origin and development of any related diseases or processes resulting in
6   premature mortality. While the substantial recent progress presented in Chapters 8 and 9 of the
7   draft CD and summarized below has provided important insights that contribute to the plausibility
8   of community study results, this more ambitious goal of understanding fundamental mechanisms
9   has not yet been reached. Some of the more important findings presented therein, including those
10   related to the cardiovascular system, may be more accurately described as intermediate responses
11   potentially caused by PM exposure rather than complete mechanisms. It appears unlikely that the
12   complex mixes of particles that are present in community air pollution would act alone though any
13   single pathway of response. Accordingly, it is plausible that several responses might occur in
14   concert to produce reported health endpoints.
15   By way of illustration, Mauderly et al. (1998) examined prevalent hypotheses related to
16   PM health effects that have been under consideration, in order to guide PM monitoring programs.
17   They produced an illustrative list of 11 components/characteristics of interest for which some
18   evidence existed. The list included: 1) PM mass concentration, 2) PM particle size/surface area,
19   3) ultrafine PM, 4) metals, 5) acids, 6) organic compounds, 7) biogenic particles, 8) sulfate and
20   nitrate salts, 9) peroxides, 10) soot, and 11) co-factors, including effects modification or
21   confounding by co-occurring gases and meteorology. The authors stress that this list is neither
22   definitive nor exhaustive, and note that "it is generally accepted as most likely that multiple toxic
23   species act by several mechanistic pathways to cause the range of health effects that have been
24   observed" (Mauderly et al., 1998).
25   In assessing the more recent animal, controlled human, and epidemiologic information, the
26   draft CD developed a summary of current thinking on pathophysiological mechanisms for the
27   effects of low concentrations of particulate air pollution (CD, pp. 8-72 to 8-77, pp. 9-89 to 9-94).
28   The potential mechanisms discussed in the draft CD, organized by effects category, are
29   reproduced in Table 3-1 below.

1 **Table 3-1. Summary of Current PM Mechanism Hypotheses** (CD, pp. 8-72 to 8-77, pp. 9-
2 89 to 9-94)
3

Effect	Potential Mechanisms
Direct Pulmonary Effects	Lung injury and inflammation
	Increased susceptibility to respiratory infections
	Increased airway reactivity and asthma aggravation
Systemic Effects Secondary to Lung Injury	Impairment of heart function by lowering blood oxygen levels and increasing the work of breathing
	Lung inflamation and cytokine production leading to systemic hemodynamic effects
	Increased risk of heart attacks and strokes because of increased blood coagulability secondary to lung inflamation
	PM/lung interactions potentially affecting hematopoiesis
Direct Effects on the Heart	Heart rate variability
	Autonomic control of the heart and cardiovascular system
	Uptake of particles and/or distribution of soluble components into the systemic circulation

10   The CD discussion highlights portions of the recent information that serve as support for

11 these effects categories and potential mechanisms. The relative support for these

12 hypotheses/intermediate effects and their relevance to real world inhalation of ambient particles

13 varies significantly. Moreover, some variability of results exist among different approaches,

14 investigators, animal models, and even day-to-day within studies. The list of hypotheses in Table

15 3-1 was developed mainly in reference to effects from short-term rather than long-term exposure

16 to PM. Repeated occurrences of some short-term insults, such as inflammation, might contribute

17 to long-term effects, but wholly different mechanisms might also be important in the development

18 of chronic responses. Even where clear mechanisms cannot be specified, however, the increasing

19 laboratory evidence of the pathways by which particles apparently affect the respiratory and

1   cardiovascular systems adds to the plausibility that particles, alone or in combination with

2   pollutant gases, are playing a causal role in the effects observed in epidemiological studies.

3   Substantial new toxicologic information outlined in the draft CD as supporting these

4   mechanisms relates to evidence for the occurrence of lung injury and inflammation and

5   intermediate effects on the heart with exposure to PM. Numerous animal toxicological studies

6   have provided clear evidence that lung injury and inflammation occur with exposure to residual oil

7   fly ash (ROFA). While this model particle is reflective of a real world combustion product, it is

8   rich in acidic metals, and its occurrence in contemporary U.S. atmospheres is limited. It has been

9   useful in elucidating the importance of metal interactions in producing inflamation. More relevant

10   evidence for inflammation has been reported in some, but not all, studies using CAPs or instilled

11   ambient particles. Most of the CAPs studies reflect the effects of fine particles between 0.2 to 2

12   um, and exclude both the ultrafine and coarse fractions. Costa and Dreher (1997) summarized

13   evidence from studies showing increased inflammatory cell counts with instillation to ambient

14   particles collected in U.S., Canadian, and German cities, and Brain et al. (1998) showed that

15   similar levels of acute inflammatory injury were caused by urban air particles and Kuwaiti oil fire

16   particles (on an equal mass basis). In one new controlled human exposure study, Ghio et al.

17   (2000) reported increased neutrophil counts and elevated levels of blood fibrinogen in lavage fluid

18   from healthy volunteers after exposure to CAPs.

19   ROFA administration has caused more severe inflammatory effects in animals, including

20   increased lung permeability which could lead to reduced oxygenation of the blood (CD, p. 9-91).

21   However, the draft CD finds that, based on studies where CAPs were used, severe disturbances

22   of oxygenation or pulmonary function by ambient PM are unlikely (CD, p. 9-91). *In vitro*

23   studies provide support for the observed inflammatory effects on ambient PM and constituent

24   substances, in finding evidence of reactive oxidant species that can damage lung cells. Several

25   studies of ambient particles (e.g. Utah Valley ambient samples) showed that soluble extracts

26   (including metals) are responsible for oxidant generation, release of IL-8 and IL-6, and PMN

27   influx (CD, p 8-48). Inflammatory changes in the lung could lead to systemic effects, in that

28   elevated levels of inflammatory cytokines (e.g., interleukin-8) in the respiratory system result in

1   cardiovascular effects. To date however, no studies have shown a clear-cut link between changes

2   in cardiovascular function and production of cytokines in the lung (CD, p. 8-75).

3   Lung inflammation could also lead to increased blood coagulability that increases the risk

4   of heart attacks and strokes. It is widely known that increased coagulability of the blood is linked

5   to increased risk of heart attacks (CD, p. 9-92). Some toxicological and epidemiological studies

6   have shown that ambient PM exposure can result in increased levels of fibrinogen (Ghio et al.,

7   2000; Peters al., 2000) or plasma viscosity (Peters et al., 1997), but Godleski et al. (2000) and

8   Seaton et al. (2000) did not report similar changes in fibrinogen or clotting-related blood factors.

9   Animal studies have provided initial evidence that high particle concentrations can have

10 systemic, especially cardiovascular, effects (CD, p. 8-34). In response, recent epidemiology

11 studies have begun to include more sensitive measures of cardiovascular responses. An

12 increasingly coherent picture is emerging of linkages between ambient PM and such responses.

13 An integrated discussion of this evidence is presented below in Section 3.3.3.3. Several potential

14 mechanisms of relevance to such effects, involving secondary responses to PM effects on the

15 lung, are noted above in Table 3-1. The draft CD also poses possible mechanisms for direct

16 effects on the heart. Inhaled PM could affect autonomic control of the heart and cardiovascular

17 system, with resulting changes in heart rate or heart rate variability. Also, inhaled PM could affect

18 the heart or other organs if particles or particle constituents are released into the circulatory

19 system from the lungs, although this remains somewhat speculative.

20 In conclusion, dosimetric information shows that both fine- and coarse-fraction particles

21 (smaller than 10 µm) can penetrate and deposit in the tracheobronchial and alveolar regions of the

22 lung. Particles also may carry other harmful substances with them to these regions, with the

23 smaller particles having the greatest surface area available for such transport (see Chapter 2

24 above). While a variety of responses to constituents of ambient PM have been hypothesized to

25 contribute to the reported health effects, there is no currently accepted mechanism(s) as to how

26 relatively low concentrations of ambient PM may cause the health effects that have been reported

27 in the epidemiological literature. Nevertheless, a substantial and growing base of recent

28 experimental studies is providing important new insights. The draft CD concludes that "[t]he

29 newer experimental evidence, therefore, adds considerable support for interpreting the

1 epidemiologic findings discussed below as being indicative of causal relationships between

2 exposures to ambient PM and consequent associated increased morbidity and mortality risks."

3 (CD, p. 9-40). The continued emphasis on these lines of research should provide important

4 insights on mechanisms for the next standards review.

5

6 **3.3   NATURE OF EFFECTS**

7 The 1996 Staff Paper identified the following key health effects categories associated with

8 PM exposure (EPA, 1996b, pp V-8 and V-9):

9 •   Increased mortality

10 •   Indices of morbidity associated with respiratory and cardiovascular disease

11   •   Hospital admissions and emergency room visits

12   •   School absences

13   •   Work loss days

14   •   Restricted activity days

15   •   Effects on lung function and symptoms

16   •   Morphological changes

17   •   Altered host defense mechanisms

18 Additional evidence is now available to identify the following new indices of morbidity:

19   •   Physicians' office or clinic visits

20   •   Effects on cardiovascular function indicators, such as heart rate variability

21   In considering the nature of effects, it is important to note some key characteristics and

22 limitations of the kinds of studies used to identify them. The general strengths and weaknesses of

23 epidemiology studies were discussed in detail in the 1996 CD (Chapter 12) and are briefly

24 reviewed in Section 6.1 of the draft CD. Epidemiology studies can identify associations between

25 actual community-level air pollution containing PM and population-level health effects, and can

26 provide evidence useful in making inferences with regard to the causality of such relationships,

27 although they cannot alone be used to demonstrate mechanisms of action. Epidemiological

28 studies can also provide information that can help to identify sensitive populations particularly at

29 risk for effects (summarized below in Section 3.4).

1   A central issue in the analysis of epidemiological evidence considered throughout the

2   discussion of effects in this section (and further in Section 3.5) is the role of co-pollutants as

3   potential confounders or effect modifiers in associations between health effects and PM. In

4   addition, co-pollutants may act as indicators for fine particles derived form specific combustion

5   sources; for example, the CD for CO concluded that ambient CO may be a surrogate for air

6   pollution from combustion sources (EPA, 2000a). Confounding occurs when a health effect that

7   is caused by one risk factor is attributed to another variable that is correlated with the causal risk

8   factor; epidemiological analyses attempt to adjust or control for potential confounders. A

9   gaseous co-pollutant (e.g., O_3, CO, SO_2 and NO_2) meets the criteria for potential confounding in

10   PM-health associations if: (1) it is a potential risk factor for the health effect under study; (2) it is

11   correlated with PM; and (3) it does not act as an intermediate step in the pathway between PM

12   exposure and the health effect under study (CD, p. 6-4).   Effect modifiers include variables that

13   may influence the health response to the pollutant exposure (e.g., co-pollutants, individual

14   susceptibility, smoking or age); epidemiological analyses do not attempt to control for effect

15   modifiers, but rather to identify and assess the level of effect modification (CD, p. 6-4). Other

16   important issues and uncertainties involved in evaluating epidemiological studies are related to the

17   role of various components within the fine and coarse fractions, as well as various analytical issues

18   including lag periods, model specification, measurement error, and various exposure periods

19   (summarized below in Section 3.5).

20   Animal toxicology, controlled human exposure, and dosimetry studies can provide

21   important support to epidemiological studies and can help elucidate biological mechanisms that

22   explain observed effects (discussed above in Section 3.2). Such studies can also provide

23   important information on risk factors for individual or population susceptibility to effects and on

24   characteristics of particles (e.g., constituents and subclasses) that may play key roles in the

25   production of health effects. However, as discussed in more detail in Chapter 8 of the draft CD,

26   the doses used in animal studies are generally much higher than community-level concentrations,

27   and important differences in dosimetry can exist across species. As a result, such studies can

28   result in animal models that may not mirror human health responses. Further, controlled human

29   exposure studies can only address the least severe health endpoints, for obvious ethical reasons,

1   and the need remains to link effects observed in such studies under simulated exposure conditions

2   (e.g., with regard to chemical composition, particle size, and concentration) to those that would

3   likely occur in real-world environments.

4   Recognizing the different strengths and limitations of these various kinds of studies, key

5   evidence illustrating these major PM effects categories is outlined below, with an emphasis on the

6   most recent information. Mortality effects are discussed in section 3.3.1, with discussion of

7   indices of morbidity in section 3.3.2, organized into three general categories: increased hospital

8   admissions and emergency room visits, effects on the respiratory system, including all other

9   morbidity indices except those related to the cardiovascular system, which are discussed

10   separately as the third category. Finally, the consistency and coherence of the overall body of

11   evidence showing associations between health effects and exposure to fine- and coarse-fraction

12   PM, alone and in combination with other pollutants, is discussed in section 3.3.3, reflecting an

13   integration of information across effects categories and disciplines, and consideration of the role

14   of gaseous co-pollutants.

15

16   **3.3.1 Premature Mortality**

17   This section discusses (1) mortality associations with short-term PM exposure, with

18   emphasis on results from newly available multi-city analyses, (2) associations with long-term PM

19   exposure, and (3) issues related to interpreting the results of mortality studies, including mortality

20   displacement and life shortening.

21   **3.3.1.1 Mortality and Short-term PM Exposure**

22   Historical reports of dramatic pollution episodes have provided clear evidence of mortality

23   associated with high levels of PM and other pollutants, as summarized in the 1996 CD (EPA,

24   1996a, pp. 12-28 to 12-31) and Staff Paper (EPA, 1996b, p. V-11). More recently, associations

25   between increased daily mortality and PM have been reported at much lower PM concentrations

26   in a large number of areas with differing climates, PM composition, and levels of gaseous co-

27   pollutants. The 1996 CD summarized about 35 time-series mortality studies using various PM

1   indicators; the majority of these studies reported positive, statistically significant[2] associations for

2   PM_{10}, as well as for $PM_{2.5}$ and other indicators of fine-fraction particles (e.g., sulfates and H^+).

3   Significant associations were reported for total mortality[3] for PM_{10} and indicators of fine-fraction

4   particles (EPA, 1996b, Tables V-3, V-11, V-12) and cause-specific mortality (i.e., respiratory-

5   and cardiovascular-related mortality) in the general population and in the elderly for PM_{10} (EPA,

6   1996b, Table V-4). In the 1996 CD, one daily mortality study addressed coarse-fraction particles

7   ($PM_{10-2.5}$), reporting no statistically significant association across the six cities included in the

8   study, although a significant association was reported in one of the six cities (EPA, 1996b, Table

9   V-14).

10   In the previous PM NAAQS review, much consideration was given to the effects of PM

11   and co-pollutants, acting alone and in combination, in the associations with adverse health effects

12   reported in epidemiological studies. The 1996 CD evaluated the findings of studies that used

13   single- and multiple-pollutant models to assess the potential for co-pollutant confounding and

14   effects modification. In some studies, PM effect estimate sizes were relatively unchanged when

15   gaseous pollutants were included in the models, and where the estimate was reduced, it typically

16   remained statistically significant (EPA, 1996a, p. 13-57). Much attention was focused on a series

17   of analyses and reanalyses using data from one U.S. city, Philadelphia, the most comprehensive of

18   which was a study funded by the Health Effects Institute (HEI). This study reported associations

19   between mortality and TSP and other pollutants, concluding that it was difficult to distinguish the

20   effects of TSP from one or more gaseous co-pollutants for this single location due in part to the

21   fact that the co-pollutants were generally correlated with TSP. Indeed, the limitations of even the

22   most comprehensive single-city analyses precluded definitive conclusions concerning the role of

23   PM. For this reason, both the 1996 CD and Staff Paper examined the consistency and coherence

24   of effects across studies of individual cities having different pollutant mixtures, climate, and other

25   factors. Based on the consistent positive associations found in such multiple studies, the CD

---

[2]Unless otherwise noted, statistically significant results are reported at a 95% confidence level.

[3]In these discussions, "total" mortality represents mortality from all causes excluding accidents and suicides, as the term is typically used in epidemiological studies on mortality and air pollution.

1   concluded that PM effects were not sensitive to other pollutants and the "findings regarding the

2   PM effects are valid" (CD, p 13-57, SP, p V-56).

3   Taking into account these findings, the HEI Oversight Committee recommended that

4   future research into the role of co-pollutants should improve upon the examination of multiple

5   single city studies by different investigators by conducting multi-city studies, using consistent

6   analytical approaches across cities, noting that "[c]onsistent and repeated observations in locales

7   with different air pollution profiles can provide the most convincing epidemiological evidence to

8   support generalizing the findings from these models" (HEI, 1997, p. 38).

9   Since the last review, more than 70 new time-series daily PM-mortality studies have been

10   published (Table 6-1 of the draft CD), including several multi-city studies that are responsive to

11   the recommendations from the last review.   The draft CD notes that with only a few exceptions,

12   these newly reported associations are generally positive, many are statistically significant (using

13   both single- and multi-pollutant models), and the reported effects estimates are generally

14   consistent with the range of estimates from the last review (CD, p. 9-44).   Drawing from the

15   current draft CD and the 1996 CD, Appendix A, Table 1, summarizes increased daily mortality

16   effects estimates for increments of PM_{10}, $PM_{2.5}$, and $PM_{10-2.5}$ from all available multi-city and

17   single-city U.S. and Canadian studies[4] as a consolidated reference for the following discussion of

18   associations between daily PM and increased total and cause-specific mortality.

19   **3.3.1.1.1 Multi-city Studies of Total Daily Mortality**

20   In considering the body of evidence on associations between PM and mortality in this

21   standards review, the multi-city studies are of particular relevance.   The multi-city studies

22   combine data from a number of cities that may vary in climate, air pollutant sources or

23   concentrations, and other potential risk factors.   The advantages of multi-city analyses include: (1)

24   evaluation of associations in larger data sets can provide more precise effects estimates than

25   pooling results from separate studies; (2) consistency in data handling and model specification can

26   eliminate variation due to study design; (3) effect modification or confounding by co-pollutants

---

[4] Findings of U.S. and Canadian studies are more directly applicable for the review of the PM NAAQS, though all study results are considered in the overall review of new scientific information. For consistency across studies, the effects estimates summarized in Appendix A, Table 1, are from single-pollutant models.

1   can be evaluated by combining data from areas with differing air pollutant combinations; (4)

2   regional or geographical variation in effects can be evaluated; and (5) "publication bias" or

3   exclusion of reporting of negative or nonsignificant findings can be avoided (CD, p. 6-39).

4   In the previous review, a single multi-city study evaluated associations between daily

5   mortality and PM, including fine- and coarse-fraction particles for six U.S. cities (Schwartz et al.,

6   1996). Significant increases in total mortality of 4.0% and 3.8% were reported per 25 $\mu g/m^3$ and

7   50 $\mu g/m^3$ of $PM_{2.5}$ and PM_{10}, respectively, while $PM_{10-2.5}$ was not significantly associated with

8   mortality. Two new analyses of the six-city data have reported results consistent with the findings

9   reported by Schwartz and colleagues (Klemm and Mason, 2000; Laden et al., 2000). The role of

10   gaseous co-pollutants was not directly addressed in any of these analyses.

11   Several new multi-city analyses, discussed below, provide valuable new insights on

12   associations between PM and mortality, including more direct evaluation of the role of co-

13   pollutants in PM-mortality associations through the use of multi-pollutant modeling.

14   The National Morbidity, Mortality and Air Pollution Study (NMMAPS) included analyses

15   of PM_{10} effects on mortality in 90 U.S. cities, with additional, more detailed, analyses being

16   conducted in a subset of the 20 largest U.S. cities (discussed below in sections on cause-specific

17   mortality and morbidity) (Samet et al., 2000a,b,c; Domenici et al., 2000). A uniform

18   methodology was used to evaluate the relationship between mortality and PM_{10} for the different

19   cities, and the results were synthesized to provide a combined estimate of effects across the cities.

20   These analyses are "marked by extremely sophisticated approaches addressing issues of

21   measurement error biases, co-pollutant evaluations, regional spatial correlation, and synthesis of

22   results from multiple cities by hierarchical Bayesian meta-regressions and meta-analyses" (CD, p.

23   6-39, 6-40).

24   As seen in Figure 3-1, the overall risk estimate for all cities is a statistically significant

25   increase of 2.3% in total mortality per 50 $\mu g/m^3$ increase in PM_{10} lagged one day[5] (Samet et al.,

26   2000a,b). Further, PM_{10} was also positively associated with mortality at 0-day and 2-day lags. In

27   two additional reports on analyses using data from the 20 largest U.S. cities, reported increases in

---

[5]Note that Figure 3-1 includes results for 88 cities in the continental U.S.; Anchorage, AK and Honolulu, HI are not included.

1   total mortality per 50 $\mu g/m^3$ increase in PM_{10} were 1.9% (Domenici et al., 2000) and 2.6% (Samet

2   et al., 2000c).

3   Also seen in Figure 3-1 are the results based on a regional assessment of these cities,

4   using seven U.S. regions. Samet et al. (2000a,b) report that some variability in effects can be seen

5   across cities and between regions. As seen in Figure 3-1, effect estimates for individual cities

6   vary; some are even negative, though not statistically significant. In addition, combined effect

7   estimates for each of the seven U.S. regions varied, with generally higher effects reported in the

8   Northeast States (a 4.5% increase in total mortality per 50 $\mu g/m^3$ increase in PM_{10} lagged one

9   day) and in Southern California. Data on some county-specific variables (e.g., mean household

10   income, percent of people not graduating from high school, percent of people using public

11   transportation) were included in analyses to investigate regional differences, but the investigators

12   did not identify any factors that might explain the apparent differences (CD, p. 6-43).

13   Notable variability in effects estimates across the 90 cities in this study would not be

14   unexpected when taking into account the study design that included many locations for which the

15   sample size (in terms of population and amount of PM_{10} data) was inherently smaller for a given

16   study period. To further examine the observed variability, the draft CD presents the 90-city effect

17   estimates plotted against the natural log of mortality-days (a product of each city's daily mortality

18   rate and the number of days for which PM data were available) as an indicator of the statistical

19   power of the analysis of each individual city (Figure 3-2). Traditionally, sample size is an

20   important factor in assessing the statistical power of a study, and, in time-series studies, the extent

21   of the time series is one measure of sample size, as is the number of health events per day (or

22   alternative time interval). In the multi-stage analyses, the NMMAPS investigators used several

23   weighting methods in combining estimates from the individual cities. As seen in Figure 3-2, cities

24   with the greatest weight or statistical power tended to have more precise effect estimates (with

25   narrower confidence intervals), and these effect estimates were generally positive
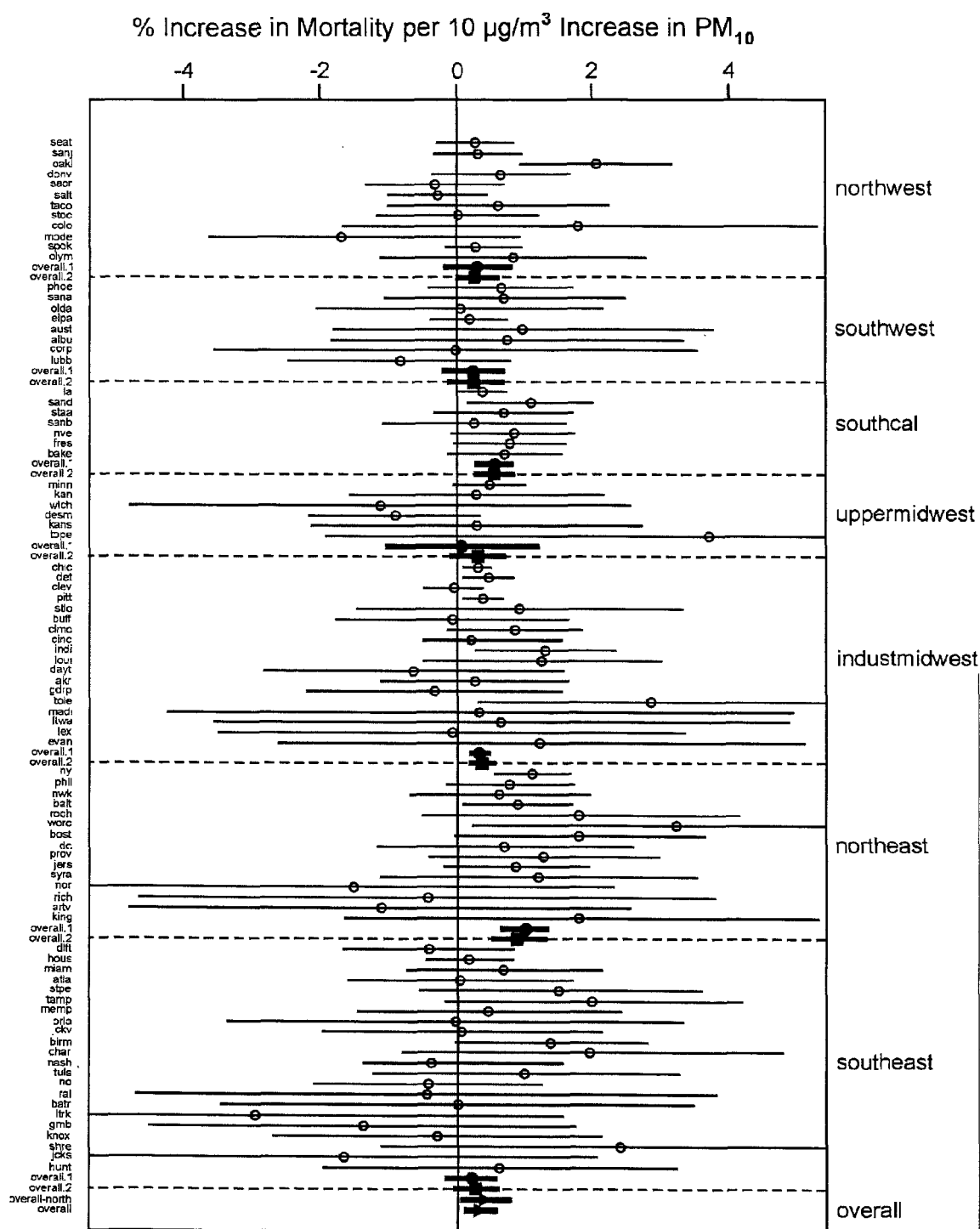
Figure 3-1. PM₁₀-mortality effects estimates for the 88 largest U.S. cities as shown in the original NMMAPS report. From Samet et al. (2000a,b). (CD Figure 6-1).

1   and statistically significant. The draft CD concludes that this "suggests some relationship between

2   effect size and study weight, overall" (CD, p. 6-212), indicating that variation in study power may

3   be a factor in explaining the apparent variation in effects estimates across cities. The draft CD

4   also presents these relationships on a regional basis (Figure 6-13, p. 6-262), suggesting that

5   further examination of these relationships may reveal interesting new insights into factors that may

6   account for any apparent intra- and inter-regional disparities (CD, p. 263).

7   One key objective of the NMMAPS analysis was to characterize the effects of PM_{10} and

8   each of the gaseous co-pollutants, alone and in combination. An important result of this

9   assessment is the finding that the associations reported between PM_{10} and mortality in the 90-city

10 analyses were not confounded by the presence of the gaseous co-pollutants (Samet et al., 2000b).

11 As seen in Figure 3-3, the effect of inclusion of other pollutants in this model on the association

12 between PM_{10} and mortality ranges from small to modest, and importantly does not affect the

13 statistical significance of the PM_{10} estimates. Significant single-pollutant associations were

14 reported for mortality for three of the gaseous co-pollutants (CO, NO_2 and SO_2), and a significant

15 association was reported for O_3 in the summer. The effects of the gaseous pollutants were,

16 however, generally diminished in multi-pollutant models that included PM_{10} (CD, p. 6-222). The

17 effects of CO alone were generally positive and significant, but adjustments for other pollutants

18 tended to reduce the effect. The authors concluded that "[t]his figure suggests that the effect of

19 PM_{10} is robust to the inclusion of other pollutants." (Samet et al., 2000b, p. 19).

20   Schwartz (2000a) conducted a series of multi-city analyses using data from 10 U.S. cities

21 where every-day PM monitoring data were available (in many areas, PM is monitored on a 1-in-3

22 or 1-in-6 day basis). Using inverse variance weighting methods to combine results across cities, a

23 statistically significant association was reported between PM_{10} and mortality, with an effect

24 estimate of a 3.4% increase per 50 $\mu g/m^3$ PM_{10}, and effect estimate sizes were the same in

25 summer and winter (CD, p. 6-44). This study also included the use of an alternative analytical

26 approach to assess confounding by co-pollutants. This approach uses data from multiple

27 locations and assesses whether there is an association between the PM effect estimate and the

28 PM-gaseous pollutant relationship in each location. A statistical relationship is first developed
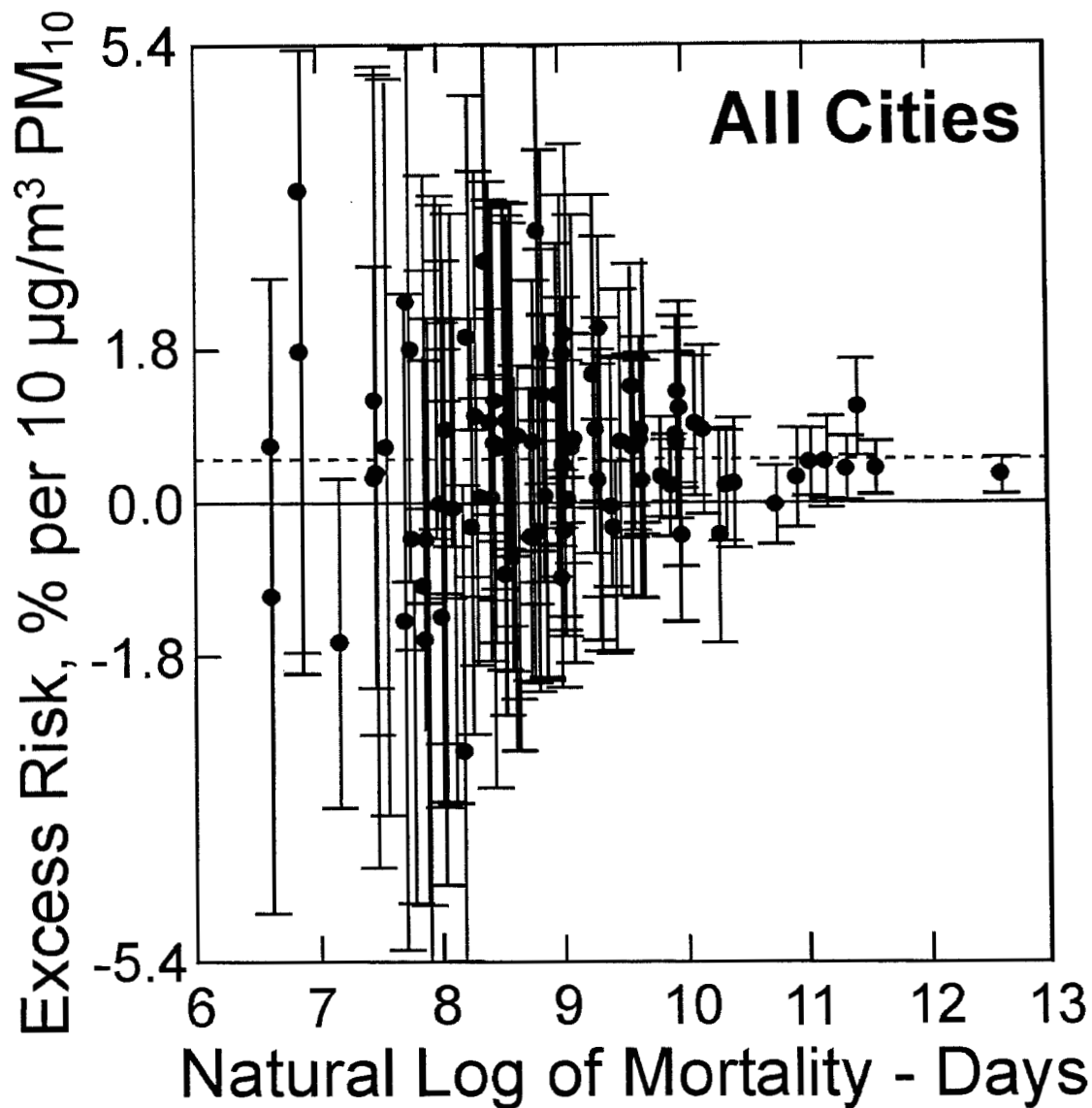
Figure 3-2. The EPA-derived plot showing relationship of PM_{10} total mortality effects estimates and 95% confidence intervals for all cities in the Samet et al. (2000a,b) NMMAPS 90-cities analyses in relation to study size (i.e., the natural logarithm of numbers of deaths times days of PM observations). Note generally narrower confidence intervals for more homogeneously positive effects estimates as study size increases beyond about the log 9 value (i.e., beyond about 8,000 deaths-days of observation). The dashed line depicts the overall nationwide effect estimate (grand mean) of approximately 0.5% per 10 $\mu g/m^3$ PM_{10} (CD Figure 6-12).
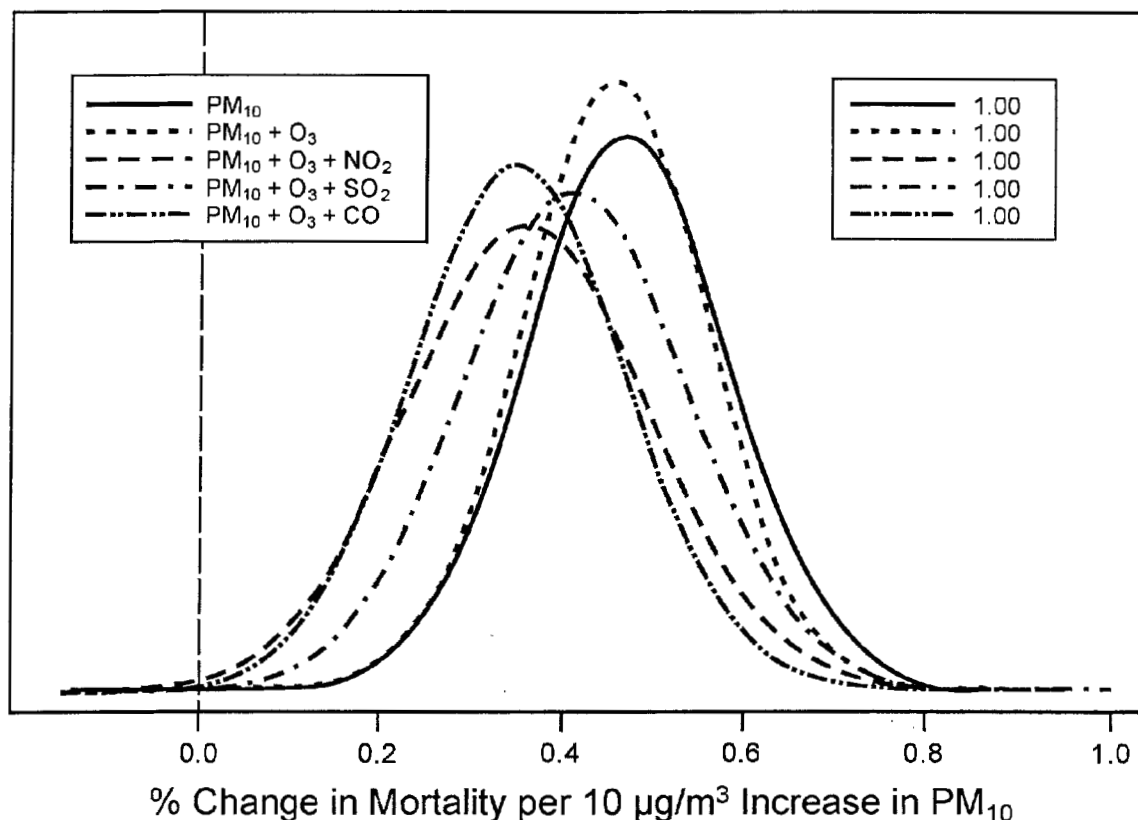
Figure 3-3. Marginal posterior distributions for effect of PM_{10} on total mortality at lag 1 with and without control for other pollutants, for the 90 cities. The numbers in the upper right legend are the posterior probabilities that the overall effects are greater than 0. (From CD Figure 6-10)

Source: Samet et al. (2000a,b).

1   for PM and the co-pollutant, then in multi-stage modeling, the PM-health model includes

2   adjustment for the PM-co-pollutant correlation. The expectation is that, if an association with

3   PM is really due to confounding by another pollutant, there would be a trend toward larger effects

4   being found in areas where the coefficient between PM and the other pollutant is larger (CD, p. 6-

5   225). No relationship was reported between PM_{10}-mortality associations and coefficients between

6   PM_{10} and O_3, CO, or SO_2, suggesting a lack of confounding by co-pollutants.

1   Further analyses of subsets of the 10 U.S. cities investigated additional research questions,

2   including the form of the concentration-response function and assessment of possible effect

3   thresholds, and the influence of influenza epidemics on PM-mortality relationships (Schwartz,

4   2000a,b,d; Schwartz and Zanobetti, 2000; Zanobetti and Schwartz, 2000; and Braga et al., 2000).

5   These findings will be discussed further as each topic is addressed in this chapter.

6   In a combined analysis of data for the 8 largest Canadian cities, Burnett et al. (2000)

7   reported that mortality was significantly associated with both $PM_{2.5}$ and PM_{10}, but not $PM_{10-2.5}$.

8   Overall effect estimates for increased total mortality of 3.0% and 3.5% were reported per 25

9    $\mu g/m^3$ and 50 $\mu g/m^3$ increases in $PM_{2.5}$ and PM_{10}, respectively. Additional analyses were

10   conducted using $PM_{2.5}$ components, including sulfates and a number of metals, and these results

11   are discussed further in Section 3.5.2. The Canadian 8-city study also showed that the

12   associations between mortality and $PM_{2.5}$ and PM_{10} generally remained significant in a number of

13   analyses when gaseous co-pollutants and 0- and 1-day lags were included in the models, although

14   in a few instances the effects estimates were reduced and lost statistical significance. The authors

15   conclude that mortality is associated with both PM and gaseous pollutants (Burnett et al., 2000).

16   In addition, a European multi-city study, Air Pollution and Health: A European Project

17   (APHEA), has resulted in a series of analyses that were summarized in the draft CD (pp. 6-47 to

18   6-49). Although the studies used consistent analytical methodologies, the PM measurement

19   methods varied between cities, including TSP, BS, PM_{13}, and PM_{10}, thus making the quantitative

20   comparisons with U.S. and Canadian findings more difficult. Significant associations between

21   various measures of PM and mortality were reported in some overall analyses, with differences

22   reported between regions. The effects estimates reported for western cities, approximately 2%

23   increase in mortality per 50 $\mu g/m^3$ PM_{10}, are consistent with those reported in U.S. and Canadian

24   studies, but no significant associations were reported with data from central or eastern European

25   countries. The APHEA investigators postulated a number of potential reasons for variation

26   between regions, such as differences in exposure representativeness, pollution mix, sensitive sub-

27   population proportions, or model fit for seasonal control (CD, p. 6-48).

28   The results from each of the U.S. and Canadian multi-city studies are summarized in Table

29   3-2 (including the two reanalyses of data from six U.S. cities used in Schwartz et al., 1996). The

1   draft CD notes that the combined daily mortality estimates from these multi-city studies are all
2   consistent with the range of PM_{10} effects estimates reported in the last review (CD, p. 6-49) (i.e.,
3   1.5% to 8.5% per 50 $\mu g/m^3$ PM_{10}), with the 90-city estimate toward the lower end of the range.
4   Further, similarly sized effect estimates are reported between total mortality and PM_{10} and $PM_{2.5}$,
5   but no significant associations are reported with $PM_{10-2.5}$.

TABLE 3-2. RESULTS OF U.S. AND CANADIAN MULTI-CITY STUDIES ON ASSOCIATIONS BETWEEN SHORT-TERM PM EXPOSURE AND MORTALITY

Study	% Increase in Mortality per 50 $\mu g/m^3$ $PM_{15/10}$	% Increase in Mortality per 25 $\mu g/m^3$ $PM_{2.5}$	% Increase in Mortality per 25 $\mu g/m^3$ $PM_{10-2.5}$	Range of City PM Mean Levels ($\mu g/m^3$)
Six U.S. Cities *Schwartz et al.,* *1996*	*4.04 (2.53, 5.62)*	*3.79 (2.77, 4.82)*	*1.00 (-0.37, 2.40)*	*PM_{10} 17.8-45.6* *$PM_{2.5}$ 11.2-29.6* *$PM_{10-2.5}$ 6.6-16.1*
Six U.S. Cities (reanalysis) Klemm and Mason, 2000	4.08 (2.78, 5.36)	3.28 (2.27, 4.31)	1.00 (-0.37, 2.40)	$PM_{15/10}$ medians 14.4-30.3 $PM_{2.5}$ medians 9.0-23.1 $PM_{10-2.5}$ medians 5.0-13.0
Six U.S. Cities (new analysis) Laden et al., 2000	---	4.05 (2.78, 5.34)	---	$PM_{2.5}$ NR
90 U.S. Cities Samet et al., 2000a,b	2.27 (0.10, 4.48)	---	---	PM_{10} 15.3-52.0
10 U.S. Cities Schwartz et al., 2000	3.40 (2.65, 4.14)	---	---	PM_{10} 27.1-40.6
8 Canadian Cities Burnett et al., 2000	3.51 (1.04, 6.04)	3.03 (1.10, 4.99)	1.82 (-0.72, 4.43)	PM_{10} 20.4-31.0 $PM_{2.5}$ 9.5-17.7 $PM_{10-2.5}$ 8.9-16.8

1   In summary, the findings of the Six-Cities study that was available during the previous

2   review have been confirmed by new analyses, and powerful new multi-city analyses have provided

3   important new evidence showing associations between daily mortality and changes in PM_{10} and

4    $PM_{2.5,}$ alone and in combination with gaseous co-pollutants routinely present in the ambient air.

5   ### 3.3.1.1.2 Other Studies of Total Daily Mortality

6   Numerous studies have been conducted in single cities or locations in the U.S. or Canada

7   (summary of results in Appendix A, Table 1), as well as locations in Europe, Mexico City, South

8   America, Asia or Australia (summary of results in Table 6-1 of the draft CD). As was observed

9   based on the more limited studies available in the last review, the associations reported in the

10   recent studies on PM_{10} and mortality are largely positive, and frequently statistically significant.

11   Similarly, a number of new studies also provide evidence of statistically significant associations

12   with $PM_{2.5}$. In contrast, statistically significant associations were not generally reported for PM_{10-}

13   $_{2.5}$. Using the same approach taken in the CD in presenting the NMMAPS results (Figure 3-2),

14   the results of U.S. and Canadian single-location and multi-city analyses for mortality with PM_{10},

15   $PM_{2.5}$, and $PM_{10-2.5}$ (using single-pollutant model results) are plotted in Figures 3-4, 3-5 and 3-6,

16   respectively. Effect estimates are plotted in order of increasing study power or weight, and, as

17   seen in Figure 3-2, there is the expected tendency for results of studies with greater power to have

18   more precise effect estimates. Along with the new study findings, each figure includes effect

19   estimates for studies included in the 1996 CD and, for comparison purposes, the range of

20   statistically significant effect estimates from the previous review. Effect estimates for total,

21   cardiovascular and respiratory mortality are included to give an overview of the entire body of

22   mortality studies, though cause-specific findings will be discussed further in the next section.

23   A number of new single-city analyses have included multi-pollutant modeling for

24   evaluating effects of PM and co-pollutants. As was found in the previous review, some of these

25   analyses report that PM effect sizes are little affected by the inclusion of co-pollutant gases in the

26   models, while others report potential confounding by one or more co-pollutants. In U.S. studies

27   conducted in Coachella Valley and Santa Clara County, California and Detroit, Michigan,

28   investigators concluded that generally positive associations (both significant and non-significant)

29   between PM and mortality were relatively unchanged in multi-pollutant models (Ostro et al.,

1   1999, 2000; Lippmann et al., 2000; Fairley, 1999). As in the previous review, some of the new

2   single-city studies found evidence of confounding. In the U.S., based on analyses in Cook, Los

3   Angeles, and Maricopa Counties, Moolgavkar (2000a) reported that the inclusion of gaseous co-

4   pollutants resulted in large reductions in PM effect estimates.

5   As seen in Figures 3-4 and 3-5, associations between total mortality and both PM_{10} and

6    $PM_{2.5}$ are generally positive and many reach statistical significance, especially in those studies with

7   greater study power or weight. For both, the results of the larger studies show quantitative

8   consistency in findings between studies, as well as with the ranges of statistically significant

9   effects estimates from the 1996 CD. The range of findings among the smaller studies is greater

10   with a few fairly large effects estimates, some of which attain statistical significance, but with

11   much larger confidence intervals. In contrast, few significant associations were reported with

12   $PM_{10-2.5}$ (Figure 3-6), with none occurring among the studies with greater power.

13   While some of the studies conducted in Europe, Mexico or South America use gravimetric

14   PM measurements (e.g., PM_{10}, $PM_{2.5}$, $PM_{10-2.5}$), many of the non-North American studies use PM

15   indicators such as TSP, BS or COH, and the Australian studies use nephelometric measures of

16   PM. As summarized in Table 6-1 of the draft CD, these studies also show largely positive,

17   significant associations between PM and mortality. While effect estimates for different PM

18   indicators may not be quantitatively comparable, the results from all of these studies taken

19   together show qualitative consistency in finding significant associations between changes in PM

20   and daily mortality.
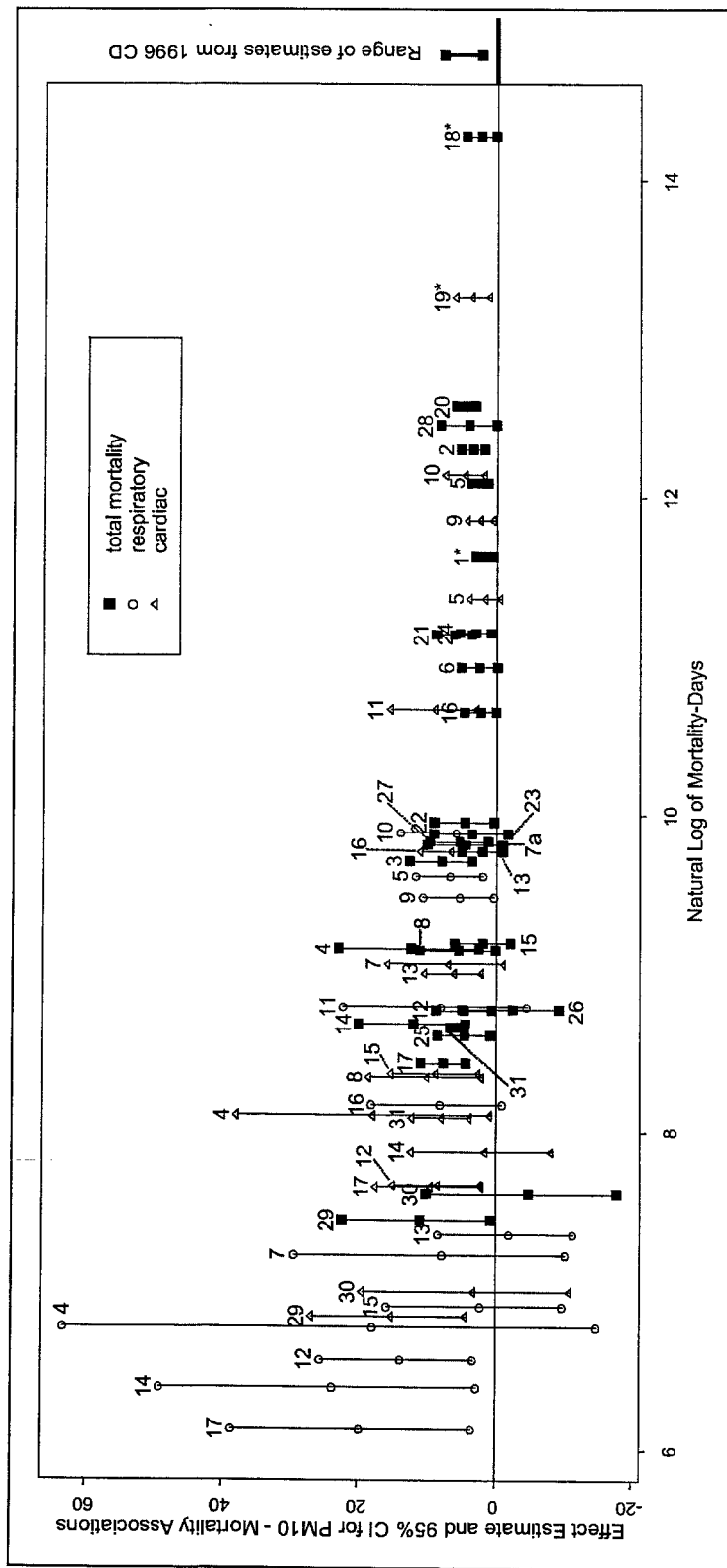
Figure 3-4. Effects estimates for PM_{10} and mortality from total, respiratory and cardiovascular causes from U.S. and Canadian cities in relation to study size, in terms of the natural log of the mortality-days product (the product of study days and the number of deaths per day) as an indicator of study weight, or power. Note that the study findings become more precise and quantitatively consistent as study power increases. Multi-city studies denoted with an asterisk above; study locations are identified below (data in Appendix 3-A, Table 4A)

1. Burnett et al., 2000, 8 Canadian cities
2. Burnett et al., 1998, Toronto
3. Fairley, 1999, Santa Clara
4. Gwynn et al., 2000, Buffalo
5. Ito and Thurston, 1996, Chicago
6. Kinney et al., 1995, LA
7. Lippmann et al., 2000, Detroit
8. Mar et al., 2000, Phoenix

9. Moolgavkar, 2000a, Cook Co
10. Moolgavkar., 2000a, LA
11. Moolgavkar., 2000a, Maricopa
12. Ostro et al., 1999, Coachella Valley
13. Ostro et al., 2000, Coachella Valley
14. Pope et al., 1999, Ogden
15. Pope et al., 1999, Provo/Orem
16. Pope et al., 1999, Salt Lake City

17. Pope et al., 1992, Utah Valley
18. Samet et al., 2000b, 90 U.S. city
19. Samet et al., 2000c, 20 U.S. city
20. Schwartz and Zanobetti, 2000, Chicago
21. Schwartz et al., 1996, Boston
22. Schwartz et al., 1996, Knoxville
23. Schwartz et al., 1996, Portage
24. Schwartz et al., 1996, St. Louis

25. Schwartz et al., 1996, Steubenville
26. Schwartz et al., 1996, Topeka
27. Schwartz,, 1993, Birmingham
28. Styer et al., 1995, Chicago
29. Tsai et al., 2000, Camden NJ
30. Tsai et al., 2000, Elizabeth NJ
31. Tsai et al., 2000, Newark NJ

3-25   Do Not Cite or Quote

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Figure 3-5. Effects estimates for $PM_{2.5}$ and mortality from total, respiratory and cardiovascular causes from U.S. and Canadian cities in relation to study size, in terms of the natural log of the mortality-days product (the product of study days and the number of deaths per day) as an indicator of study weight, or power. Note that the study findings become more precise and quantitatively consistent as study power increases. Multi-city studies denoted with an asterisk above; study locations are identified below (data in Appendix A, Table 4)

1. Burnett et al., 2000, 8 Canadian cities
2. Burnett et al., 1998, Toronto
3. Fairley, 1999, Santa Clara
4. Goldberg et al., 2000, Montreal
5. Lippmann et al., 2000, Detroit

6. Mar et al., 2000, Phoenix
7. Moolgavkar., 2000a, LA
8. Ostro et al., 1995, So. California
9. Ostro et al., 2000, Coachella Valley
10. Schwartz 2000c, Boston

11. Schwartz et al., 1996, Boston
12. Schwartz et al., 1996, Knoxville
13. Schwartz t al., 1996, Portage
14. Schwartz et al., 1996, St. Louis
15. Schwartz et al., 1996, Steubenville

16. Schwartz et al., 1996, Topeka
17. Tsai et al., 2000, Camden NJ
18. Tsai et al., 2000, Elizabeth NJ
19. Tsai et al., 2000, Newark NJ

Figure 3-6. Effects estimates for $PM_{10-2.5}$ and mortality from total, respiratory and cardiovascular causes from U.S. and Canadian cities in relation to study size, in terms of the natural log of the mortality-days product (the product of study days and the number of deaths per day) as an indicator of study weight, or power. Note that the study findings become more precise and quantitatively consistent as study power increases. Multi-city studies denoted with an asterisk above; study locations are identified below (data in Appendix 3-A, Table 4C)

1. Burnett et al., 2000, 8 Canadian cities
2. Fairley, 1999, Santa Clara
3. Lippmann et al, 2000, Detroit

4. Mar et al., 2000, Phoenix
5. Ostro et al., 2000, Coachella Valley
6. Schwartz et al., 1996, Boston.

7. Schwartz et al, 1996, Knoxville
8. Schwartz et al., 1996, Portage
9. Schwartz et al, 1996, St. Louis

10. Schwartz et al., 1996, Steubenville
11. Schwartz et al., 1996, Topeka

| 1 | ### 3.3.1.1.3 Cause-specific Daily Mortality |

1   ### 3.3.1.1.3 Cause-specific Daily Mortality

2   In the 1996 Staff Paper, several studies also reported associations between PM_{10} and

3   respiratory and cardiovascular mortality (EPA, 1996b, p. V-13). The associations reported with

4   mortality from respiratory or cardiovascular diseases were generally consistent with the results for

5   total mortality, and the CD concluded that this lent support to the biological plausibility of the PM

6   associations (EPA, 1996a, p. 12-69). If particles have effects on the respiratory or cardiovascular

7   systems, it would be expected that associations reported for total mortality reflect the underlying

8   associations with cardiorespiratory[6] mortality and not be influenced by deaths from non-

9   cardiorespiratory causes (EPA, 1996a, p. 12-77).

10   Figures 3-4, 3-5, and 3-6 shown above present findings for PM_{10}, $PM_{2.5}$ and $PM_{10-2.5}$,

11   respectively, from U.S. and Canadian studies, where it can be seen that there is general

12   consistency between effects estimate ranges for mortality from total, respiratory and

13   cardiovascular causes. In general, as was observed in the 1996 CD, some of the effect estimates

14   for respiratory mortality are larger in magnitude but less precise, with large confidence intervals,

15   which is likely because respiratory-related deaths comprise a small proportion of daily mortality

16   rates.

17   A number of studies have evaluated associations for both total and cause-specific

18   mortality. The recent U.S. multi-city study, NMMAPS, included a comparison of findings for

19   total and cardiorespiratory mortality for the 20 largest U.S. cities. The effect estimate for deaths

20   from cardiorespiratory causes was somewhat larger (3.5% increase per 50 $\mu g/m^3$ increase in

21   PM_{10}) than that for deaths from all causes (2.6% increase per 50 $\mu g/m^3$ increase in PM_{10}) (Samet

22   et al., 2000c). In the results of individual studies, as summarized in Appendix A, Table 1, effects

23   estimates for mortality from respiratory and cardiovascular causes tend to be larger than those for

24   total mortality, though these comparisons are not readily apparent in Figures 3-4 through 3-6

25   when combined with all study results. For example, Tsai et al. (2000) also report

26   cardiorespiratory mortality effect estimates with $PM_{2.5}$ and PM_{15} that are somewhat larger than

27   those for total mortality. For respiratory and cardiovascular mortality, nearly all of the U.S. and

---

[6] "Cardiorespiratory" refers to cardiovascular and respiratory diseases, combined, and is used here as an equivalent term to "cardiopulmonary".

1	Canadian studies show somewhat larger effects estimates than for total mortality associations with
2	PM_{10} and $PM_{2.5}$ (e.g., Gwynn et al., 2000; Ostro et al., 1999; Pope et al., 1999; Fairley, 1999;
3	Lippmann et al., 2000; Mar et al., 2000; Goldberg et al., 2000) (results in Appendix A, Table 1).
4	As was found with total mortality, few significant associations were reported with $PM_{10-2.5}$ for
5	cause-specific mortality; however, in those few studies, the effects estimates for cardiovascular
6	mortality tended to be greater than those for total mortality (Mar et al., 2000; Ostro et al., 2000).
7	In NMMAPS analyses, a positive, but not statistically significant, association was also
8	reported with "other" or non-cardiorespiratory deaths (Samet et al., 2000c). In some analyses
9	where "other" causes of death were evaluated, no associations with PM were reported (Ostro et
10	al., 1999, 2000). Some associations between PM and "other" mortality were reported in a Detroit
11	study (Lippmann et al., 2000), but the draft CD observes "that the 'other' mortality showed
12	seasonal cycles and apparent influenza peaks, suggesting that this series may have also been
13	influenced by respiratory contributing causes" (CD, p. 6-72). In Montreal, fine PM was
14	associated with "other nonaccidental causes" of death, but when analyses included more specific
15	"other" causes, significant associations were reported only for diabetes, which typically also
16	involves cardiovascular complications as it progresses (Goldberg et al., 2000). The draft CD
17	concludes, "at least some of these 'other' associations may also be due to seasonal cycles that
18	include relationships to peaks in influenza epidemics that may imply respiratory complications as a
19	'contributing' cause to the 'other' deaths. Or, the 'other' category may include sufficient
20	numbers of deaths due to diabetes or other diseases which may also involve cardiovascular
21	complications as contributing causes." (CD, p. 6-75).
22	In addition to the evidence from epidemiology studies, new, though limited, information is
23	available from toxicology studies that offers insight into PM-related mortality. In some of the
24	toxicology studies summarized in Chapter 8 of the draft CD, animals died after exposure to PM or
25	PM surrogates, though none of these studies was designed to assess lethality. For example, some
26	studies have used monocrotaline-treated rats as a model for individuals with cardiorespiratory
27	disease, and "have demonstrated that intratracheal instillation of high levels of ambient particles
28	can increase or accelerate death related to monocrotaline administration in rats" (CD, p. 8-25).
29	Indicators of inflammation or cardiac arrhythmia were also measured in these studies (CD, Table
30	8-7). While the suitability of this animal model may be questioned, the findings offer some

1   evidence of plausibility to the associations with cardiorespiratory mortality reported in

2   epidemiology studies. Since the studies were designed to assess effects on cardiovascular or

3   respiratory systems, the toxicological evidence for PM-related effects is more fully discussed in

4   the sections on respiratory and cardiovascular systems effects.

5   In summary, the new studies continue to report risks for mortality from cardiovascular and

6   respiratory diseases with increasing PM, and the findings suggest that associations reported for

7   total mortality are indicative of associations with deaths from cardiorespiratory-related causes.

8   **3.3.1.2 Mortality and Long-term PM Exposure**

9   The 1996 CD summarized the findings of a number of cross-sectional studies that had

10   been conducted over the past several decades. These studies had identified associations between

11   increased mortality and residence in communities with higher pollution levels, but concern was

12   raised about the lack of information on potentially important covariates and methodological

13   limitations (EPA, 1996a, p. 12-159). Results were also available from three more recent

14   prospective cohort studies (i.e., the Six Cities, American Cancer Society (ACS), and California

15   Seventh Day Adventist (ASHMOG) studies) that included subject-specific information on

16   potential confounders (e.g., smoking history, occupation, health history) and were considered to

17   provide more reliable results (EPA, 1996a, p. 13-33).

18   The strongest evidence from the prospective cohort studies was reported for associations

19   with fine particles. The ACS study reported significant associations for $PM_{2.5}$ and sulfates (a fine

20   particle surrogate). The Six Cities study evaluated effects of many PM size classes, and

21   significant associations were reported with PM_{15}, $PM_{2.5}$, sulfates and non-sulfate fine particles, but

22   not with TSP or coarse particles (TSP-PM_{15} or PM_{15}-$PM_{2.5}$) (EPA, 1996a, Table 12-18). Both

23   the Six Cities and ACS studies reported associations with mortality from all causes and

24   cardiorespiratory causes, with larger effects estimates for cardiorespiratory causes. The

25   AHSMOG study did not find an association between TSP and mortality. The CD concluded that

26   the chronic exposure studies, taken together, suggested associations between increases in

27   mortality and long-term exposure to PM (EPA, 1996a, p. 13-34).

28   The new studies that are available for the current review include a comprehensive

29   reanalysis and extended analyses of data from the Six Cities and ACS studies (Krewski et al.,

30   2000) and new analyses using updated data from the AHSMOG study (Abbey et al., 1999).

1   Findings from the original Six Cities, ACS, and AHSMOG investigations together with those

2   from new studies and reanalyses are summarized in Table 3-3.

3   The reanalysis of the Six Cities and ACS studies included two major components, a

4   replication and validation study, and a sensitivity analysis, where alternative risk models and

5   analytic approaches were used to test the robustness of the original analyses. In the first phase,

6   the Investigators reported the data from the two studies to be of generally high quality, and was

7   able to replicate the original results, confirming the original investigators' findings of associations

8   with both total and cardiorespiratory mortality (CD, p. 6-83).

9   The sensitivity analyses generally reported that the use of alternative models, including

10   variables that had not been used in the original analyses (e.g., physical activity, lung function,

11   marital status), did not materially alter the original findings. The Investigators also obtained data

12   on additional city-level variables that were not available in the original data sets (e.g., population

13   change, measures of income, maximum temperature, number of hospital beds, water hardness)

14   and included these data in the models. The associations between fine particles and mortality were

15   generally unchanged in these new analyses, with the exception of population change, which did

16   somewhat reduce the size of the associations with fine particles or sulfates.

17   Further analyses were conducted using data for potentially susceptible subgroups, and the

18   results did not show differences in the PM-mortality associations between most subgroups,

19   including gender, smoking status, exposure to occupational dusts and fumes, and marital status.

20   However, the effects of fine particles appeared to be larger in the subgroup without a high school

21   education than with more education; the Investigators postulated that this relationship could be

22   due to some unidentified socioeconomic effect modifier.

TABLE 3-3. EFFECT ESTIMATES PER INCREMENTS[A] IN LONG-TERM MEAN LEVELS OF FINE AND INHALABLE PARTICLE INDICATORS FROM U.S. AND CANADIAN STUDIES

Type of Health Effect & Location	Indicator	Change in Health Indicator per Increment in PM	Range of City PM Levels * Means ($\mu g/m^3$)
Increased total mortality in adults		Relative Risk (95% CI)	
Six City[B]	$PM_{15/10}$ (20 $\mu g/m^3$)	1.18 (1.06-1.32)	18-47
	$PM_{2.5}$ (20 $\mu g/m^3$)	1.28 (1.09-1.51)	11-30
Six City[C]	$PM_{15-2.5}$ (20 $\mu g/m^3$)	1.43 (0.82-2.47)	range = 9.7
ACS Study[D] (151 U.S. SMSA)	$PM_{2.5}$ (20 $\mu g/m^3$)	1.14 (1.07-1.21)	9-34
Six City Reanalysis[E]	$PM_{15/10}$ (20 $\mu g/m^3$)	1.19 (1.06-1.34)	18.2-46.5
	$PM_{2.5}$ (20 $\mu g/m^3$)	1.28 (1.09-1.51)	11.0-29.6
ACS Study Reanalysis[E]	$PM_{15/10}$ (20 $\mu g/m^3$) (SSI)	1.02 (0.99-1.04)	34-101
	$PM_{2.5}$ (20 $\mu g/m^3$)	1.14 (1.08-1.21)	9.0-33.4
	$PM_{15-2.5}$ (20 $\mu g/m^3$)	1.01 (0.97-1.05)	9-42
	$PM_{2.5}$ (20 $\mu g/m^3$)	1.14 (1.08-1.21)	9.0-33.4
Southern California[F]	PM_{10} (20 $\mu g/m^3$)	1.01˙(0.92, 1.10)**	51 (±17)
	PM_{10} (cutoff= 30 d/yr >100 $\mu g/m^3$)	0.99 (0.93, 1.06)**	
	$PM_{2.5}$ (24.3 $\mu g/m^3$)	1.22 (0.95, 1.58) (males)	31.9 (17.2-45.2)
	$PM_{10-2.5}$ (9.7 $\mu g/m^3$)	1.05 (0.92, 1.20) (males)	27.3 (3.7, 44.3)

* Range of mean PM levels given unless, as indicated, studies reported overall study mean (min, max), or mean (±SD)
** represents pooled estimates for males and females, using inverse weighted variances

[A]Results calculated using PM increment between the high and low levels in cities, or other PM increments given in parentheses

References:
[B]Dockery et al. (1993)
[C]EPA, (1996a)
[D]Pope et al. (1995)
[E]Krewski et al. (2000)
[F]Abbey et al. (1999)

Adapted from CD Tables 6-11 and 9-6.

1   It has been recognized that pollution levels have declined over time in many areas. When

2   some key risk factors, including pollution level, were allowed to vary over time in the analyses, it

3   was found that the association between fine particles and mortality was reduced, but remained

4   statistically significant. This might be expected, if the most polluted cities had the greatest decline

5   in pollutant levels as controls were applied (CD, p. 6-85).

6   The original analyses had not included assessment of co-pollutant confounding, though

7   single-pollutant analyses between mortality and the co-pollutant gases were done in the Six Cities

8   analysis. Significant or borderline significant associations were reported with SO_2 and NO_2, but it

9   was observed that these pollutants were strongly correlated with PM (CD, p. 12-168). The

10   Investigators obtained additional data on gaseous pollutant concentrations and evaluated both the

11   effects of these pollutants alone and with PM in multi-pollutant models. Significant associations

12   were reported between mortality and sulfur dioxide, and in multiple pollutant models, the sulfur

13   dioxide associations often appeared stronger than those for fine particles and sulfates. The

14   authors suggest that it is more likely that sulfur dioxide is acting as a marker for other mortality-

15   associated pollutants, and conclude "Nonetheless, both fine particles and sulfate continued to

16   demonstrate a positive association with mortality even after adjustment for the effects of sulfur

17   dioxide in our spatial regression analyses." (Krewski et al., 2000, p. 233, 234)

18   Several methods were used to address variation from city to city, or spatial correlation

19   among cities, using the larger sulfate data set. The resulting sulfate associations were sometimes

20   smaller and sometimes larger than the original effect estimate. The Investigators concluded: "it

21   suggests that uncontrolled spatial autocorrelation accounts for 24% to 64% of the observed

22   relation. Nonetheless, all our models continued to show an association between elevated risks of

23   mortality and exposure to airborne sulfate." (Krewski et al., 2000, p. 228).

24   In summary, the draft CD concluded that the reanalysis generally confirmed the original

25   investigators' findings of associations between mortality and long-term exposure to fine particles.

26   As seen in draft CD Table 6-6, the mortality relative risk estimates reported in the replication

27   analysis were nearly identical to those reported in the original studies (CD, p. 6-84). In the

28   sensitivity analyses, Krewski et al. (2000) reported risk estimates that were "remarkably robust to

29   alternative risk models" (p. 25). While recognizing that increased mortality may be attributable to

1   more than one component of ambient air pollution, the reanalysis confirmed the association

2   between mortality and fine particle and sulfate exposures (CD, p. 6-87).

3   Analyses of the AHSMOG cohort available for the 1996 CD reported no significant

4   associations between mortality and PM, measured as TSP (Abbey et al., 1991). In the new

5   studies discussed in the draft CD (pp. 6-87 to 6-99), analyses have used more recent air quality

6   data for PM_{10} and have estimated $PM_{2.5}$ concentrations from visibility data. A significant

7   association was reported for total mortality and PM_{10} (number of days exceeding 100 $\mu g/m^3$) for

8   males (CD, p. 6-88), but no significant associations were reported for other PM_{10} indices (e.g., 30

9     $\mu g/m^3$ increase), for deaths from contributing respiratory causes, and among females. Additional

10   analyses were conducted using only data from males and estimated $PM_{2.5}$ and $PM_{10-2.5}$

11   concentrations; larger effects estimates were reported for mortality with $PM_{2.5}$ than with $PM_{10-2.5}$,

12   but again, the estimates were generally not statistically significant (CD, Table 6-10). The draft

13   CD concludes that the "lack of consistent findings in this study does not cast doubt on the

14   findings of the Six Cities and ACS studies, which both had larger study populations (especially the

15   ACS study), were based on measured PM data (in contrast with AHSMOG PM estimates based

16   on TSP or visibility measurements) and have been validated through an exhaustive reanalysis."

17   (CD, p. 6-94).

18   An additional new long-term exposure study has been recently published (Lipfert et al.,

19   2000b). The study examines a prospective cohort of military men assembled by the Veterans

20   Administration in the 1970s. The investigators report inconsistent and largely nonsignificant

21   associations between PM exposure (including, depending on availability, TSP, PM_{10}, $PM_{2.5}$, PM_{15}

22   and $PM_{15-2.5}$) and mortality. The draft CD finds "it is difficult to assess the methodological

23   soundness of this study or to interpret its preliminary results. The findings may reflect one or

24   more unintentional forms of confounding" (CD, p. 6-101). The final model used by the authors

25   included 233 variables, of which 162 were interaction terms of systolic blood pressure, diastolic

26   blood pressure, and body mass index variables with age. The blood pressure variables may be an

27   important intermediate step in the causal pathway between PM and cardiorespiratory health

28   effects, and it is generally inappropriate to treat factors in the causal pathway as confounders (CD,

29   p. 6-100 and 6-101). In summary, the CD concludes that the results of this study do not cast

30   doubt on the results of the Six Cities, ACS and reanalysis studies.

1   In addition to the analyses of total and cardiorespiratory mortality described above, the

2   three prospective cohort studies examined PM in relation to lung cancer mortality. None of the

3   three studies (Six Cities, ACS, AHSMOG) reported a significant association between long-term

4   exposure to fine particles and lung cancer mortality (EPA, 1996b, p. V-17). The reanalysis study

5   confirmed these findings for the Six Cities and ACS studies (Krewski et al., 2000). One new

6   study on potential lung cancer associations has used data from the AHSMOG cohort. As

7   summarized in the draft CD, significant associations were reported between long-term PM_{10}

8   exposure and lung cancer mortality for males, but not females; some associations were also

9   reported with other gaseous pollutants. The findings were based on a small number of lung

10   cancer deaths in the cohort, and the effect estimates were quite variable, with some described as

11   "high non-credible RR [relative risk]" (CD, p. 6-91). Further analysis using data for males and

12   estimated $PM_{2.5}$ and $PM_{10-2.5}$ reported no statistically significant associations with lung cancer

13   mortality for either $PM_{2.5}$ or $PM_{10-2.5}$ (CD, p. 6-92). Thus, there remains little evidence for lung

14   cancer associations with ambient PM mass.

15   A few new studies have linked infant mortality with average ambient PM concentrations

16   over periods of one month or more during gestation or around the time of birth. Each of the

17   studies reviewed in the draft CD (Section 6.2.3.4) reported significant associations between infant

18   mortality and PM exposure. One recent U.S. study reported significant associations between

19   PM_{10} concentrations during the first 2 months of the infant's life and mortality from respiratory

20   causes and sudden infant death syndrome (Woodruff et al., 1997). Studies conducted in the

21   Czech Republic and Mexico City also find associations with infant mortality, and the CD

22   concludes that these findings "suggest that infants may be among sub-populations notably affected

23   by long-term PM exposure" (CD, p. 6-106). Less consistent evidence was reported for an

24   association between PM exposure during gestation and low birth weight for infants (CD, p. 6-

25   102).

26   In summary, positive, statistically significant associations between mortality from total or

27   cardiorespiratory causes and fine particles were reported in the Six Cities and ACS studies and

28   these results were confirmed in an extensive reanalysis. In considering these results, as well as the

29   other evidence related to long-term exposures discussed above, the draft CD concludes that long-

1   term PM exposure durations are likely associated with serious human health effects. (CD, p. 6-267).

2   **3.3.1.3 Mortality Displacement and Life-Shortening**

3   The 1996 CD and Staff Paper discussed the issue of mortality displacement, or whether

4   some of the acute mortality associations represent deaths among the weakest individuals who

5   might have died within days even without PM exposure (sometimes referred to as "harvesting").

6   Limited data were available, and it was concluded that there may be evidence of mortality

7   displacement occurring in some portion of the population, but that further research was needed to

8   more fully address this question (EPA, 1996b, p. V-19). In its assessment of the extent of life-

9   shortening that may occur with long-term exposure to PM, the CD concluded that increased

10   mortality results from both short-term and long-term ambient PM exposure, and that the amount

11   of life shortening could potentially be on the order of years (EPA, 1996a, p. 13-45).

12   More recently, the extent to which mortality displacement may be occurring was

13   investigated using two new types of analyses. One type of study separated time-series data into

14   three components -- seasonal and longer fluctuations, intermediate fluctuations, and short-term

15   fluctuations -- and varied the cutoff between the intermediate and short-term cycles to test for the

16   presence of harvesting (Schwartz, 2000; Schwartz and Zanobetti, 2000). While there was

17   evidence in the Boston analysis that mortality from chronic obstructive pulmonary disease

18   (COPD) may be displaced by a only few months, effect sizes for deaths from pneumonia, heart

19   attacks, and all causes were reported to increase as longer time scales were included, thus offering

20   no evidence for harvesting effects. (Schwartz, 2000). Similar results were reported in the analysis

21   of data from Chicago; this study also reported that effect size increased more steeply with

22   increasing time scale for deaths outside the hospital than for in-hospital deaths (Schwartz and

23   Zanobetti, 2000). Using data from Milan, Italy, positive associations were reported between TSP

24   and mortality up to 13 days, with no effect reported in the next few days, then positive

25   coefficients from 20 days to 45 days (maximum time scale used in study), possibly providing

26   evidence for an initial "rebound" due to depletion of the susceptible population, but with an

27   overall increase in effect size when considering mortality over the longer time scale (Zanobetti et

28   al., 2000). Using first simulation analyses, then analyses using data from Philadelphia, effects of

29   harvesting were assessed at 3 days, 30 days, and 300 days (Zeger et al., 1999), and larger effect

1   sizes were reported for the longer frequency ranges. The results of these studies "suggest that the

2   extent of harvesting, if any, is not a matter of a few days" (CD, p. 6-245).

3   The extent of life-shortening that may be associated with long-term PM exposure has been

4   investigated in a recent analysis using effect estimates from existing studies and life-table analysis

5   methods (Brunekreef, 1997). Chronic exposure to PM, with an exposure difference of 10 $\mu g/m^3$,

6   was associated with a reduction in 1.31 years in the population's life expectancy at age 25.

7   Taking into account the evidence from a few new studies showing associations between infant

8   mortality and PM exposure, the draft CD finds that these data suggest that potential life-

9   shortening associated with long-term PM exposure may be even greater than Brunekreef's (1997)

10   estimate. (CD, p. 6-106).

11

12   **3.3.3   Indices of Morbidity**

13   As noted in 1996 PM Staff Paper, given the statistically significant positive associations

14   between community PM concentrations and mortality, it is reasonable to anticipate that

15   comparable epidemiological studies should find increased morbidity with elevated levels of PM

16   (EPA, 1996b, p. V-21). This was indeed the case in the past review, where positive associations

17   were reported between PM and morbidity effects ranging from the more severe (e.g.,

18   hospitalization for respiratory or cardiovascular diseases) to moderate exacerbation of respiratory

19   conditions or decreases in lung function. Staff noted the logical relationships between the cause

20   specific mortality and hospital admissions results, as well as those across the range of morbidity

21   effects and sensitive populations.

22   A number of more recent epidemiological studies also find increased hospital admissions

23   or emergency room visits, as well as changes in lung function and respiratory symptoms with PM

24   exposure. Other new epidemiology studies have expanded the range of morbidity indices of

25   morbidity associated with PM, including physicians' office or clinic visits for respiratory disease,

26   and cardiovascular health indicators such as heart rate or heart rate variability. In the previous

27   review, several epidemiology studies also reported increased numbers of school absences, lost

28   work days or restricted activity days with increased PM (EPA, 1996b, p. V-22); little new

29   evidence is provided for these morbidity indices in the draft CD.

1   The recent literature also shows productive interactions among toxicological, controlled

2   human, and epidemiological studies of morbidity effects. Effects related to some new endpoints

3   measured in the recent epidemiological studies, such as heart rate variability, were first reported in

4   animal toxicology studies. Some toxicology studies have used ambient PM samples from areas in

5   which epidemiological studies were conducted (e.g. Ghio, 1999a,b). In addition, many

6   laboratory studies have measured cellular or physiological changes, such as changes in numbers of

7   immune cell types, levels of cytokines, or measures of pulmonary or cardiovascular function

8   following exposure to CAPs or instilled ambient particles. The more subtle biological responses

9   measured in such studies may provide supporting evidence for morbidity associations reported

10   without being considered separate indices of morbidity.

11   **3.3.3.1 Hospital Admissions or Emergency Room Visits**

12   Hospitalization and emergency room visits are measures of more severe respiratory or

13   cardiovascular morbidity, and associations with these health outcomes have been evaluated in

14   numerous studies. The 1996 Staff Paper observed that epidemiological studies demonstrated

15   associations between hospital admissions and emergency room visits for respiratory and cardiac

16   causes and PM_{10} exposure (EPA, 1996b, p. V-21). Most studies evaluated relationships with

17   admissions/visits for respiratory diseases, including asthma, COPD and pneumonia, and nearly all

18   associations were statistically significant. Where multi-pollutant models were evaluated,

19   associations reported with PM_{10} were not substantially changed with the inclusion of gaseous co-

20   pollutants in the models. Several studies had also reported associations between PM and hospital

21   admissions for cardiovascular diseases. The 1996 CD included results from only one study where

22      $PM_{2.5}$ and $PM_{10-2.5}$ data were available, and associations with total respiratory admissions/visits

23   were reported for both, with the associations with fine particles or fine particle components were

24   larger and less influenced by co-pollutant confounding (Thurston et al., 1994). As noted in the

25   1996 Staff Paper, the associations reported with hospital admissions and emergency room visits

26   were coherent with the findings of significant associations with mortality, especially mortality

27   from cardiovascular and respiratory causes.

28   Numerous recent studies have continued to report significant associations between PM

29   and hospital admissions or emergency room visits for respiratory or cardiovascular diseases. The

30   new studies have included multi-city analyses, numerous assessments using cardiovascular

1   admissions/visits, and evaluation of the effects of fine- and coarse-fraction particles. The findings

2   from U.S. and Canadian studies on associations with PM_{10}, $PM_{2.5}$ or $PM_{10-2.5}$ are presented in

3   Figures 3-7, 3-8 and 3-9, respectively. In these figures, effects estimates are presented by general

4   respiratory or cardiovascular effects categories, separated into more specific subcategories in

5   cases where results from several studies are available (e.g., COPD, asthma). Within each group,

6   the results are presented in order of decreasing study size or power, using the natural log of the

7   product of study days times number of admissions/visits per day. The results for all new

8   cardiovascular and respiratory admissions/visits studies, including those using nongravimetric PM

9   measurements and studies from non-North American locations, are summarized in the draft CD in

10   Tables 6-16 and 6-17, respectively, and the effect estimates for PM_{10}, $PM_{2.5}$ or $PM_{10-2.5}$ from U.S.

11   and Canadian studies are summarized in Appendix A, Tables 2 and 3, respectively.

12   Effect estimates for PM_{10} presented in Figure 3-7 include findings from multi-city studies,

13   as well as results from studies available for review in the 1996 CD, with the range of statistically

14   significant effect estimates from the 1996 CD indicated at the right-hand margin; for $PM_{2.5}$ or

15     $PM_{10-2.5}$, the effects estimates from the only study on respiratory admissions/visits available in the

16   1996 CD are indicated in the right-hand margins in Figures 3-8 and 3-9. In general, positive,

17   mostly statistically significant associations for both respiratory and cardiovascular

18   admissions/visits are seen with PM_{10} and $PM_{2.5}$, as well as with $PM_{10-2.5}$.

19   As discussed previously, the results of multi-city studies are of particular relevance in the

20   review of PM standards. The recent U.S. multi-city study, NMMAPS, reported statistically

21   significant associations between PM_{10} and hospital admissions in the elderly for cardiovascular

22   diseases, pneumonia or COPD in 14 cities (Samet et al., 2000b), with somewhat larger effect
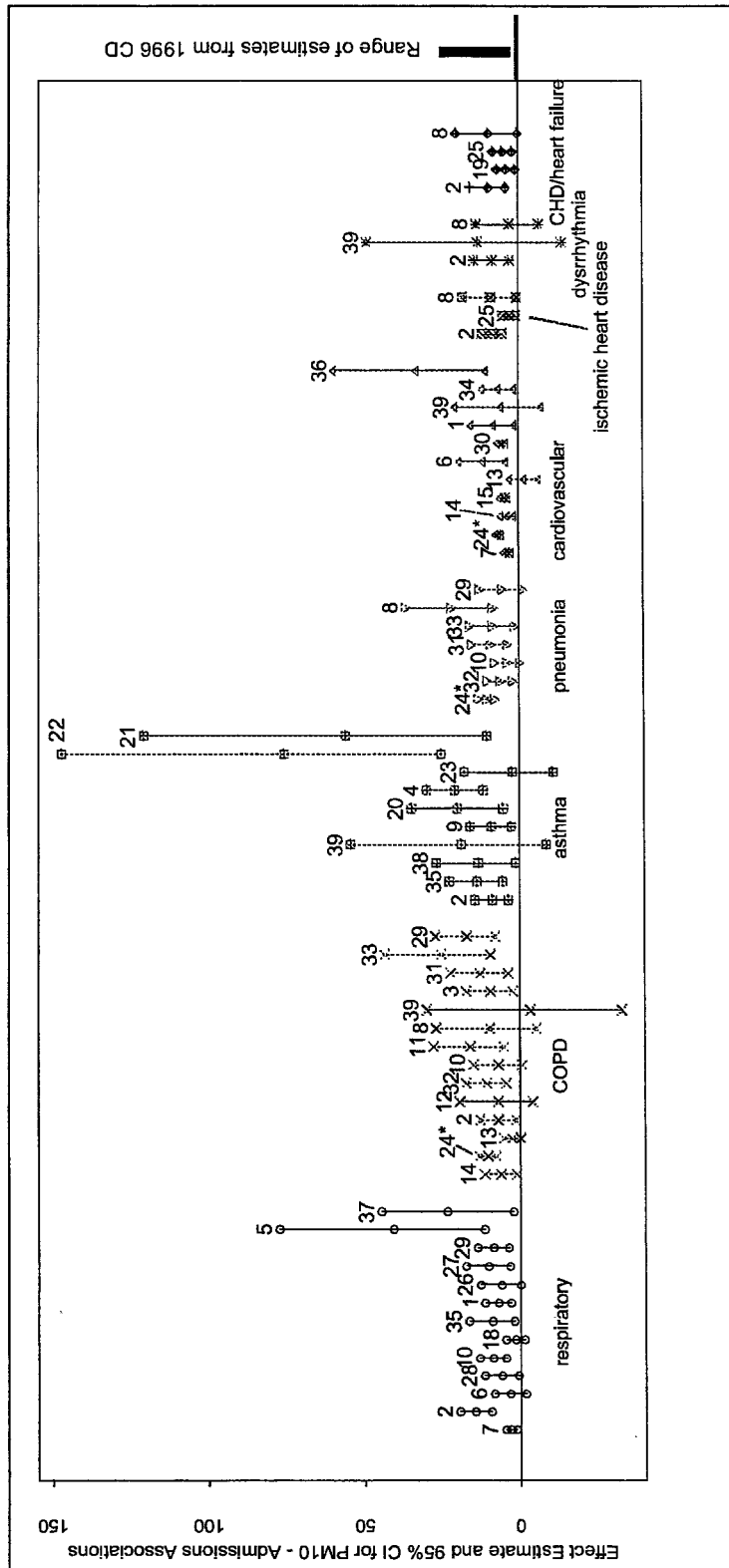
Figure 3-7. Effects estimates for PM_{10} and hospital admissions, emergency room visits (denoted ◇) or physicians office visits (denoted ⊙) for various respiratory and cardiovascular diseases from U.S. and Canadian studies. Within each category, associations are ranked by decreasing natural log of the morbidity-days product (product of study days and number of admissions/visits per day). Multi-city studies denoted with an asterisk above; study locations are identified below (data in Appendix 3-A, Table 4D)

1. Burnett et al., 1997, Toronto
2. Burnett et al., 1999, Toronto
3. Chen et al., 2000, Reno
4. Choudhury et al., 1997, Anchorage ⊙
5. Delfino et al., 1997, Montreal ◇
6. Gwynn et al., 2000, Buffalo
7. Linn et al., 2000, LA
8. Lippmann et al., 2000, Detroit
9. Lipsett et al., 1997, Santa Clara ◇
10. Moolgavkar et al., 1997, Minn/St. Paul

11. Moolgavkar et al., 2000, King Co.
12. Moolgavkar, 2000c, Maricopa Co.
13. Moolgavkar, 2000b, Maricopa Co.
14. Moolgavkar, 2000c, Cook Co,
15. Moolgavkar, 2000b, LA
16. Moolgavkar, 2000c, LA.
17. Moolgavkar, 2000b, Cook Co.
18. Moolgavkar, et al., 1997, Birmingham
19. Morris and Naumova, 1998, Chicago
20. Nauenberg and Basu, 1999, LA

21. Norris et al., 2000, Seattle ◇
22. Norris et al., 1999, Seattle ◇
23. Norris et al., 2000, Spokane ◇
24. Samet et al., 2000b, 14 U.S. cities
25. Schwartz and Morris, 1995, Detroit
26. Schwartz, 1995, New Haven
27. Schwartz, 1995, Tacoma
28. Schwartz et al., 1996, Cleveland
29. Schwartz et al., 1996, Spokane
30. Schwartz, 1999, 8 US Counties

31. Schwartz, 1994b, Birmingham
32. Schwartz, 1994a, Detroit
33. Schwartz, 1994c, Minn/St. Paul
34. Schwartz, 1997, Tucson
35. Sheppard et al., 1999, Seattle
36. Stieb et al., 2000, St. John ◇
37. Thurston et al., 1994 Toronto
38. Tolbert et al., 2000b, Atlanta ◇
39. Tolbert et al., 2000a, Atlanta ◇

Figure 3-8. Effects estimates for PM$_{2.5}$ and hospital admissions or emergency room visits (denoted ◊) for various respiratory and cardiovascular diseases from U.S. and Canadian studies. Within each category, associations are ranked by decreasing natural log of the morbidity-days product (product of study days and number of admissions/visits per day). Study locations are identified below (data in Appendix 3-A, Table 4E)

1. Burnett et al., 1997, Toronto
2. Burnett et al., 1999, Toronto
3. Delfino et al., 1997, Montreal ◊

4. Delfino et al., 1998, Montreal ◊
5. Lippmann et al., 2000, Detroit
6. Lumley and Heagerty, 1999, King Co

7. Moolgavkar et al., 2000, King Co.
8. Moolgavkar, 2000b, LA
9. Moolgavkar, 2000c, LA
10. Norris et al., 1999, Seattle ◊

11. Sheppard et al., 1999, Seattle
12. Stieb et al., 2000, St. John ◊
13. Thurston et al., 1994, Toronto
14. Tolbert et al., 2000a, Atlanta ◊
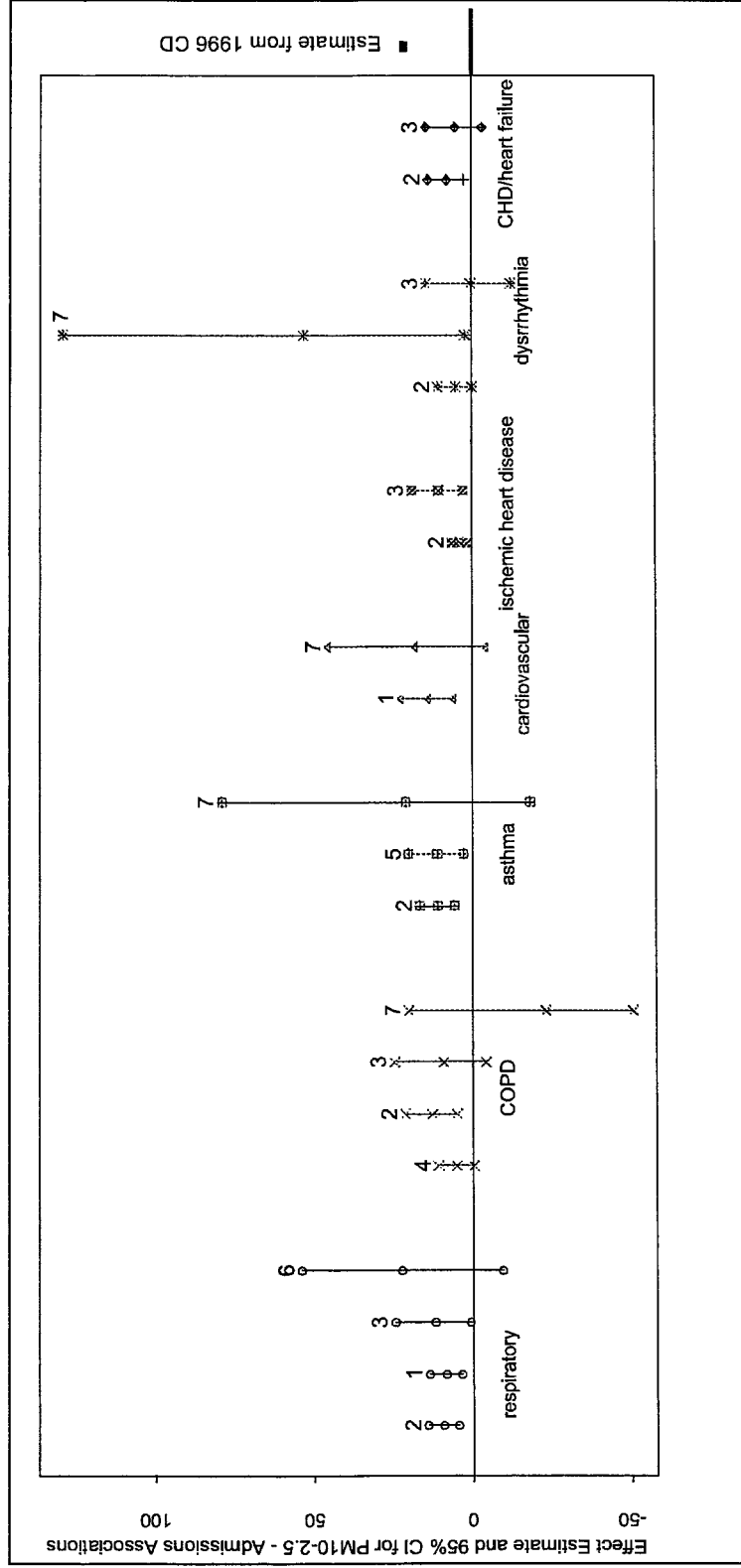
Figure 3-9. Effects estimates for $PM_{10-2.5}$ and hospital admissions or emergency room visits (denoted ◇)for various respiratory and cardiovascular diseases from U.S. and Canadian studies. Within each category, associations are ranked by decreasing natural log of the morbidity-days product (product of study days and number of admissions/visits per day). Study locations are identified below (data in Appendix 3-A, Table 4F)

1. Burnett et al., 1997, Toronto
2. Burnett et al., 1999, Toronto

3. Lippmann et al., 2000, Detroit
4. Moolgavkar, 2000b, LA
5. Sheppard et al., 1999, Seattle

6. Thurston et al., 1994, Toronto
7. Tolbert et al., 2000a, Atlanta ◇

1   estimates when a distributed lag approach was used (Zanobetti et al., 2000). Increases of 6% in

2   hospital admissions for cardiovascular disease and 10% in hospital admissions for COPD or

3   pneumonia per 50 $\mu g/m^3$ increase in PM_{10} were reported. In addition, the authors used a new

4   approach for evaluating potential confounding by testing for associations between the PM effect

5   estimate and the PM-gaseous pollutant relationship in each location (as was done in multi-city

6   mortality analyses described in Section 3.3.1.1.1). No evidence was found for trends between the

7   coefficients between PM_{10} and O_3 or SO_2 and PM_{10}-respiratory admissions associations, or

8   between the coefficients between PM_{10} and CO, O_3 or SO_2 and PM_{10}-cardiovascular admissions

9   associations, indicating that confounding by co-pollutants is unlikely (Samet et al., 2000b).

10   A multi-city study analysis for 8 U.S. counties also reported statistically significant

11   associations between PM_{10} and hospital admissions for cardiovascular diseases among the elderly.

12   An increase of 5% in admissions was associated with a 50 $\mu g/m^3$ increase in PM_{10}, with no

13   evidence of confounding with ambient CO (Schwartz, 1999).

14   In the European multi-city study, APHEA, associations between PM and admissions/visits

15   for all respiratory diseases, asthma or COPD were largely positive, though not always statistically

16   significant. While the APHEA analyses used PM measurements from a variety of methods (e.g.,

17   suspended particles, black smoke), which makes quantitative comparisons with North American

18   studies difficult, the draft CD observes that the APHEA results are qualitatively consistent with

19   results of other studies (CD, p. 6-177).

20   Considering all U.S. and Canadian studies, PM_{10} and $PM_{2.5}$ are associated with

21   admissions/visits for respiratory diseases and specific disease categories, including asthma, COPD,

22   pneumonia, and the findings are generally consistent with those reported in the 1996 CD. In Figure

23   3-7, it can be seen that most associations between PM_{10} and admissions/visits for respiratory

24   causes are positive and statistically significant. A number of new studies have also reported

25   significant associations between $PM_{2.5}$ and admissions/visits for respiratory diseases (Figure 3-8).

26   The CD concludes that the numerous recent studies provide evidence for associations with PM_{10}

27   and $PM_{2.5}$ at levels lower than had been demonstrated previously for this health outcome (CD, p.

28   6-179).

29   Though fewer studies are available, several recent studies show significant associations

30   between admissions/visits for respiratory diseases and $PM_{10-2.5}$ (Figure 3-9). In addition, the draft

1   CD observes that, as was found in the previous review, significant associations are reported

2   between PM_{10} and hospital admissions or emergency room visits for respiratory diseases in studies

3   that were conducted in areas of the western U.S. where coarse-fraction particles are predominant

4   (CD, p. 6-236), indicating a likely role for coarse-fraction particles in the reported effects. Thus,

5   both fine- and coarse-fraction particles appear to be linked to increases in hospital admissions and

6   emergency room visits for respiratory diseases, though more evidence is available for fine-fraction

7   particles. In addition, where investigators have used two-pollutant models to test the

8   independence of the effects of each size fraction, $PM_{2.5}$ and $PM_{10-2.5}$ were not highly correlated and

9   had independent effects (Lippmann et al., 2000; Moolgavkar, 2000c).

10   Figures 3-7 through 3-9 present effects estimates from single-pollutant models. As

11   discussed above, the multi-city analyses of hospital admissions have not found evidence of

12   significant confounding by co-pollutant gases. In single-city studies, a number of investigators

13   evaluated the effects of gaseous co-pollutants independently and in multi-pollutant models with

14   PM. As discussed in further detail in Section 3.5.1, some gaseous pollutants have been reported to

15   have independent effects on the respiratory system and might be expected to act as confounders in

16   PM-admissions/visits associations. For example, a number of studies have indicated that O_3 is

17   associated with increased admission/visits for respiratory diseases, such as asthma, and a number of

18   the studies in Table 6-17 of the draft CD report significant associations with O_3. In some of these

19   studies, PM effect estimates were reduced in two-pollutant models with O_3 (e.g., Tolbert et al.,

20   2000b; Delfino et al., 1998), but in others, PM associations were generally reported to be robust to

21   inclusion of O_3 in the models (e.g., Lippmann et al., 2000; Gwynn et al., 2000; Burnett et al.,

22   1997) and less evidence was found for potential confounding by other gaseous pollutants (results

23   summarized in Table 6-17 of the draft CD). In considering studies of cardiovascular

24   admissions/visits, the draft CD focused on CO as a co-pollutant of interest, due to the known

25   effects of CO on the cardiovascular system (EPA, 1999). The draft CD finds that "[t]he above

26   analyses of daily PM_{10} and CO in U.S. cities, overall, suggest that elevated concentrations of both

27   PM_{10} and CO may enhance risk of cardiovascular (CVD)-related morbidity leading to acute

28   hospitalizations" (CD, p. 6-128). In studies of cardiovascular and chronic respiratory disease

29   admissions/visits, Moolgavkar (2000b,c) reports that associations with PM were dramatically

30   reduced with the inclusion of either CO or NO_2 (differs by location and health endpoint) in the

1   models. For cardiovascular admissions/visits (but equally true for respiratory diseases) the CD

2   concludes: "In some studies, PM clearly carries an independent association after controlling for

3   gaseous co-pollutants. In others, the 'PM effects' are markedly reduced once co-pollutants are

4   added to the model; but this may in part be due to both PM and co-pollutants such as CO and NO_2

5   being emitted from a common source (motor vehicles) and consequent colinearity between them

6   and/or the gaseous pollutants such as CO having independent effects on cardiovascular function"

7   (CD, p. 6-141).

8   The CD concludes that the U.S. multi-city studies (Samet et al., 2000a,b; Schwartz, 1999)

9   likely provide the most precise estimates for relationships of U.S. ambient PM_{10} exposure to

10   increased risk for hospitalization (CD, pp. 6-127, 6-172). Taken together, the findings of new

11   studies and those reviewed in the 1996 CD offer consistent evidence for associations between

12   ambient PM concentrations and admissions/visits to the hospital or emergency room for respiratory

13   or cardiovascular diseases.

14   **3.3.3.2 Effects on the Respiratory System**

15   Evidence available in the previous review suggested associations between PM exposure

16   and respiratory effects such as changes in lung function, increases in respiratory symptoms or

17   disease, as well as related morbidity indices such as school absences, lost work days and restricted

18   activity days (EPA, 1996b, pp. V-21 and V-22). From epidemiology or controlled human

19   exposure studies of short-term PM exposure, it was reported that sensitive individuals (especially

20   those with asthma or pre-existing respiratory symptoms) may have increased or aggravated

21   symptoms, with or without reduced lung function (EPA, 1996b, p. V-23). Long-term (months to

22   years) exposure to PM was linked with decreased lung function and increased incidence of

23   respiratory diseases such as bronchitis (EPA, 1996b, p. V-26). The results of studies using long-

24   term and short-term PM exposure data were reported to be consistent with one another. In

25   addition, toxicology studies using surrogate particles or PM components, generally at high

26   concentrations, and autopsy studies of humans and animals reported evidence of pulmonary

27   effects, including morphological damage (e.g., changes in cellular structure of the airways), and

28   changes in resistance to infection.

29   Recently published studies summarized in the draft CD have included toxicological or

30   controlled human exposure studies of exposures to ambient PM, using inhalation exposures to

1   CAPs or intratracheal instillation of ambient PM samples. These studies provide additional new

2   evidence linking PM with respiratory effects. Among the many new epidemiology studies are

3   several assessing relationships between PM and additional health endpoints, including physicians'

4   office visits. A number have evaluated effects on lung function or respiratory symptoms, while few

5   new studies have assessed effects such as school absences or work loss days, which are indirect

6   measures that may be linked with respiratory illness.

7   *Acute Respiratory Effects - Epidemiological Studies.* Among the new epidemiology

8   studies are several using medical visits for respiratory illness as a measure of health effects. These

9   studies have evaluated effects of pollutant exposure on visits to physician's offices (Anchorage,

10   Alaska, Choudhury et al., 1997; London, UK, Hajat et al., 1999; Santiago, Chile, Ostro et al.,

11   1999), or doctor's visits to patients (Paris, France, Medina et al., 1997). Visits for asthma were

12   significantly increased with PM exposure in children (Medina et al., 1997) and people of all ages

13   (Choudhury et al., 1997), and significant associations were found with visits for lower respiratory

14   diseases in children (Ostro et al., 1999) and adults (Hajat et al., 1999).

15   The draft CD notes that these studies "provide new insight into the fact that there is a

16   broader scope of severe morbidity associated with PM air pollution exposure than previously

17   documented" (CD, p. 6-180). These studies find associations in a range of 3% to 42% increases in

18   medical visits with a 50 $\mu g/m^3$ change in PM_{10} (CD Table 6-17). The results of these studies offer

19   further support for coherence in effects on the respiratory tract, since they are consistent with

20   findings of increased mortality and hospital admissions or emergency room visits for respiratory

21   diseases. These new studies also indicate the potentially more widespread public health impact of

22   the less severe respiratory health endpoints (CD, p. 6-181).

23   New epidemiology studies on PM-related effects on respiratory symptoms or lung function

24   are summarized in draft CD Tables 6-19 through 6-23; the studies are grouped by health status of

25   the study subjects (asthmatic or nonasthmatic) and PM exposure (short- and long-term). Only a

26   few recent North American publications are available; the results for U.S. and Canadian studies

27   using gravimetric PM data are included in Appendix A, Table 2. Most U.S. and Canadian studies

28   used gravimetric PM data, generally PM_{10} and sometimes $PM_{2.5}$ and $PM_{10-2.5}$, and most were

29   studies using children.

1   All studies of effects in children reported significant associations with a range of respiratory

2   symptoms (e.g., cough, wheeze, shortness of breath) (Neas et al., 1995, 1996; Ostro et al., 1995;

3   Pope et al., 1991; Schwartz et al., 1994; Vedal et al., 1998). Some (Neas et al., 1999; Schwartz

4   and Neas, 2000; Vedal et al., 1998), but not all (Neas et al., 1995, 1996; Thurston et al., 1997), of

5   the North American studies also reported significant associations between PM_{10}, $PM_{2.5}$ or $PM_{10-2.5}$

6   and decreases in lung function measures (e.g., decreased peak expiratory flow rate).

7   From the limited number of studies using adults, Naeher et al. (1999) found significant

8   associations between PM_{10}, $PM_{2.5}$ and $PM_{10-2.5}$ and decreased lung function in adult women, but no

9   significant associations were found with respiratory symptoms by Ostro et al. (1991) or Pope et al.

10   (1991).

11   In those studies where $PM_{2.5}$ and $PM_{10-2.5}$ data were available, the findings suggest roles for

12   both fine- and coarse-fraction PM in reduced lung function and increased respiratory symptoms

13   (CD, p. 6-237). For example, using data from the Six Cities study, lower respiratory symptoms

14   were found to be significantly increased for children with $PM_{2.5}$ but not with $PM_{10-2.5}$, while the

15   reverse was true for cough (Schwartz and Neas, 2000). When both $PM_{2.5}$ and $PM_{10-2.5}$ were

16   included in models, the effect estimates were reduced for each, but $PM_{2.5}$ retained significance in

17   the association with lower respiratory symptoms and $PM_{10-2.5}$ retained significance in the

18   association with cough. In the last review, several studies reported significant associations

19   between symptoms or lung function changes with PM_{10} and fine particles or fine particle

20   surrogates, but no data were available for coarse-fraction particles (EPA 1996b, Table V-12). The

21   new studies continue to show effects of short-term exposure to PM_{10} and $PM_{2.5}$ and offer

22   additional evidence for associations between $PM_{10-2.5}$ and respiratory morbidity.

23   Considering also results from studies conducted outside the U.S. and Canada, the draft CD

24   finds evidence supporting increases in respiratory symptoms associated with short-term exposures

25   to PM for both asthmatic and nonasthmatic subjects, though many associations did not reach

26   statistical significance. Again, considering the full body of literature, short-term PM exposure was

27   associated with decreases in lung function (e.g., peak expiratory flow rate) in studies of asthmatics

28   (CD, p. 6-184) but little evidence was reported for associations between lung function and short-

29   term PM exposure in nonasthmatic subjects (CD, p. 6-194).

1   *Acute Respiratory Effects - Laboratory Studies.* Key toxicology or controlled human
2   exposure studies summarized in the draft CD include: (1) exposures of human volunteers in a
3   clinical setting to concentrated ambient PM; (2) animal studies with exposure to ambient PM by
4   inhalation of CAPs or intratracheal installation of ambient PM samples; and (3) *in vitro* exposures
5   to ambient particles using cells from the respiratory system (e.g., bronchial epithelial cells,
6   macrophages). The principal effects studied have been inflammatory response and other indicators
7   of lung injury.

8   Inflammatory responses in the respiratory system were reported in humans and animals
9   exposed to concentrated ambient fine particles. Although less evidence is available from studies
10   using ambient particle exposures, Costa and Dreher (1997) summarized evidence from studies
11   showing increased inflammatory cell counts with exposure to ambient particles collected in U.S.,
12   Canadian, and German cities, and Brain et al. (1998) showed that similar levels of acute
13   inflammatory injury were caused by urban air particles and Kuwaiti oil fire particles (on an equal
14   mass basis). One new controlled human exposure study also reported evidence of inflammatory
15   changes in the lung with exposure to CAPs (Ghio et al., 2000).

16   The types of effects reported included increases in neutrophils (either total number or
17   percent) in the lungs in humans (Ghio et al., 2000) and in animals (Clarke et al., 1999; Godleski et
18   al., 2000; Gordon et al., 1998; Kodavanti et al., 2000); though changes in immune cell numbers
19   haven't been observed in all studies (Gordon et al., 2000). Increased neutrophil levels have been
20   reported with ROFA exposures in animals or cell cultures (e.g., Costa and Dreher, 1997;
21   Killingsworth et al., 1997). Increases also have been reported in other immune cell types such as
22   eosinophils or alveolar macrophages (CD, Table 8-4). Increases in immune cells, again commonly
23   neutrophils, also were reported with intratracheal exposure to urban particles in animals (Brain et
24   al., 1998; Li et al., 1996, 1997; Ghio et al., 1999, Kennedy et al., 1998).

25   Other inflammatory changes reported have included changes in levels or increased release
26   of cytokines, or chemicals released as part of the inflammatory process (e.g., interleukins such as
27   IL-8). The draft CD concludes that exposure of lung cells to ambient PM, ROFA or PM
28   surrogates leads to increased production of cytokines and that the effects may be mediated, at least
29   in part, through production of reactive oxygen species (CD, p. 8-57).

1   A number of animal studies have shown that exposure to diesel exhaust particles could

2   increase the production or release of inflammatory cells, such as eosinophils (CD, p. 8-44).

3   Controlled exposures of humans to diesel exhaust particles also have resulted in increases in

4   inflammatory cells indicative of enhanced response to allergens (CD, p. 8-45). Together, the

5   human and animal studies provide evidence that particle exposures can produce inflammatory

6   changes in the respiratory system.

7   Animal studies also have reported evidence of general lung injury, including increased

8   protein levels in lung fluids with exposure to ambient particles (CD Table 8-3) or combustion-

9   related particles such as ROFA (CD, Table 8-4). One general cause of lung cell injury is the

10   production of reactive oxidant species that can damage the epithelial cells in the lung; these

11   chemicals can be produced as part of an inflammatory response to particle exposure. In *in vitro*

12   experiments, ambient PM exposures were reported to have effects that included increased release

13   of inflammatory chemicals, evidence of oxidant stress on the cells, and evidence of general cellular

14   toxicity (e.g., release of proteins) (CD Table 8-8). Several *in vitro* studies have reported evidence

15   of increased oxidative stress in lung cell cultures exposed to particles collected in Utah Valley;

16   notably, the particle doses used in these studies were only 2-3-fold greater than generally estimated

17   doses for humans breathing ambient air (Ghio et al., 1999a,b; Soukup et al., 2000). In two of

18   these studies, the transition metal content of the particles appeared to be more closely linked to

19   reported effects than the quantity of particles (Ghio et al., 1999a,b). Soukup and colleagues

20   (2000) also tested the effects of particles collected in Utah Valley, and found evidence of oxidant

21   activity with particles collected at times when a major industrial PM source was in operation, but

22   not when the industrial source was shut down. In this latter study, however, the effects did not

23   appear to be closely correlated with metal content of the particles.

24   Findings of inflammation and lung injury are generally consistent with epidemiological

25   results showing increases in respiratory symptoms or exacerbation of respiratory diseases. Some

26   epidemiological studies also have reported increased admissions/visits for respiratory infections or

27   pneumonia, and there is some toxicological evidence indicating increased susceptibility to

28   respiratory infections. The 1996 CD observed that impairment of pulmonary host defense

29   mechanisms by acidic particles was consistent with observations of increased prevalence of

30   bronchitis in communities with higher levels of acidic PM (EPA 1996a, p. 13-75). Similarly, the

1   draft CD finds evidence of altered lung responses to microbial agents, though at high PM

2   concentrations (CD, p. 8-47).

3   The epidemiology findings are consistent with those of the previous review in showing

4   associations with both respiratory symptom incidence and decreased lung function. As reported

5   previously, the evidence is somewhat stronger for changes in symptoms than lung function. The

6   findings from studies of physicians' office visits for respiratory diseases offer new evidence of

7   acute respiratory effects with exposure to ambient PM that is coherent with evidence of increased

8   respiratory symptoms and admissions/visits to the hospital or emergency room for respiratory

9   disease. While urging caution in interpreting the findings of the high-dose toxicology studies, the

10   draft CD concludes that the findings "have shown clearly that PM obtained from various sources

11   can cause lung inflammation and injury" and that "[t]he fact that instillation of ambient PM

12   collected from different geographical areas and from a variety of emission sources consistently

13   caused pulmonary inflammation and injury tends to corroborate epidemiological studies that report

14   increased respiratory morbidity and mortality associated with PM in many different geographical

15   areas and climates." (CD, pp. 8-19 and 8-20).

16   *Chronic Effects.* In the 1996 CD, only a few epidemiology studies had assessed

17   associations between long-term PM exposure and lung function changes or respiratory symptoms.

18   Among U.S. and Canadian studies, the Six Cities and 24-Cities studies had provided data

19   suggesting associations with chronic bronchitis and decreased FEV_1 or FVC in children (CD, p. 6-

20   205). In the 1996 Staff Paper, significant associations were observed between decreased lung

21   function or increased incidence of bronchitis in children with fine particles or fine particle

22   surrogates, with less evidence for associations with PM_{10}, PM_{15} or TSP (EPA, 1996b, Table V-

23   13).

24   Several new epidemiological analyses have been conducted on long-term pollutant

25   exposure effects on respiratory symptoms or lung function in the U.S.; numerous European, Asian,

26   and Australian studies have also been published. Little new evidence is available from toxicology

27   or controlled human exposure studies regarding long-term effects of PM exposure. The new U.S.

28   epidemiological studies are based on data from two main cohort studies, a study of schoolchildren

29   in 12 Southern California Communities and an adult cohort of Seventh Day Adventists

30   (AHSMOG).

1   As seen in Table 3-4, initial publications from the 12 Southern California Communities

2   childrens cohort show significant associations between long-term exposure to PM and incidence of

3   bronchitis or phlegm among the subgroup of children with asthma, though no significant

4   associations were found for the subgroups of children without asthma (McConnell et al., 1999). In

5   this study, some significant associations were also found for NO_2 and acid vapor (hydrochloric and

6   nitric acids) with incidence of bronchitis and phlegm and the authors found it difficult to distinguish

7   effects of these pollutants; no significant associations were found with ozone.

8   In another analysis using the same cohort, children who entered the cohort while in the 4th

9   grade showed, in tests conducted when these children were in the 7th grade, decreases in lung

10   function growth with increasing exposure to PM, including PM_{10}, $PM_{2.5}$, $PM_{10-2.5}$, and acid vapor

11   (hydrochloric and nitric acids) (Gauderman et al., 2000). Again, there was evidence for

12   associations with NO_2 and acid vapor but not with ozone. Two-pollutant models were tested in

13   this study, and the effect estimates for the various PM indices, NO_2 and acid vapor were generally

14   reduced in size. The authors observe that motor vehicle emissions are a major source of ambient

15   particles, NO_2 and inorganic acids and thus they were unable to identify the independent effects of

16   each pollutant (Gauderman et al., 2000, p. 1388).

17   In this study, significant associations were reported between ambient concentrations of

18   both fine and coarse fraction particles and reductions in mid-maximal expiratory flow (a measure

19   of small airways function); the effect size for $PM_{10-2.5}$ was slightly, but not significantly, larger than

20   that for $PM_{2.5}$. Growth in another lung function measure, forced vital capacity, was significantly

21   reduced with exposure to PM_{10} and acid vapor (hydrochloric and nitric acids), while associations

22   (though not statistically significant) were indicated for both $PM_{2.5}$ and $PM_{10-2.5}$ (Table 3-4;

23   Gauderman et al., 2000). While limited to two childrens' study populations, these findings are

24   consistent with those from short-term exposure studies where respiratory morbidity is associated

25   with both $PM_{2.5}$ and $PM_{10-2.5}$.

26   For adults, the 1996 CD summarized the results of a several cross-sectional studies as well

27   as one cohort study (AHSMOG), and found evidence for increased incidence of respiratory

28   diseases, especially bronchitis, with long-term PM exposure (EPA, 1996a, p. 12-197). Further

29   analyses have been done in the AHSMOG cohort, and significant decreases in lung function

30   (FEV_1) were reported only for the subgroup of males with a family history of lung disease (Abbey

TABLE 3-4. EFFECT ESTIMATES PER INCREMENTS[A] IN LONG-TERM MEAN LEVELS OF FINE AND INHALABLE PARTICLE INDICATORS FROM U.S. AND CANADIAN STUDIES

Type of Health Effect & Location	Indicator	Change in Health Indicator per Increment in PM[a]	Range of City PM Levels * Means (μg/m^3)
Increased bronchitis in children		Odds Ratio (95% CI)	
Six City[B]	*$PM_{15/10}$ (50 μg/m^3)*	*3.26 (1.13, 10.28)*	*20-59*
Six City[C]	*TSP (100 μg/m^3)*	*2.80 (1.17, 7.03)*	*39-114*
24 City[D]	*H^+ (100 nmol/m^3)*	*2.65 (1.22, 5.74)*	*6.2-41.0*
24 City[D]	*SO_4^- (15 μg/m^3)*	*3.02 (1.28, 7.03)*	*18.1-67.3*
24 City[D]	*$PM_{2.1}$ (25 μg/m^3)*	*1.97 (0.85, 4.51)*	*9.1-17.3*
24 City[D]	*PM_{10} (50 μg/m^3)*	*3.29 (0.81, 13.62)*	*22.0-28.6*
Southern California[E]	*SO_4^- (15 μg/m^3)*	*1.39 (0.99, 1.92)*	*---*
12 Southern California communities[F] (all children)	PM_{10} (25 μg/m^3) acid vapor (1.7 ppb)	0.94 (0.74, 1.19) 1.16 (0.79, 1.68)	28.0-84.9 0.9-3.2 ppb
12 Southern California communities[F] (children with asthma)	PM_{10} (19 μg/m^3) PM_{25} (15 μg/m^3) acid vapor (1.8 ppb)	1.4 (1.1, 1.8) 1.4 (0.9, 2.3) 1.1 (0.7, 1.6)	13.0-70.7 6.7-31.5 1.0-5.0 ppb
Increased cough in children		Odds Ratio (95% CI)	
12 Southern California communities[F] (all children)	PM_{10} (25 μg/m^3) acid vapor (1.7 ppb)	1.06 (0.93, 1.21) 1.13 (0.92, 1.38)	28.0-84.9 0.9-3.2 ppb
12 Southern California communities[G] (children with asthma)	PM_{10} (19 μg/m^3) PM_{25} (15 μg/m^3) acid vapor (1.8 ppb)	1.1 (0.0.8, 1.7) 1.3 (0.7, 2.4) 1.4 (0.9, 2.1)	13.0-70.7 6.7-31.5 1.0-5.0 ppb
Increased obstruction in adults			
Southern California[H]	PM_{10} (cutoff of 42 d/yr >100 μg/m^3)	1.09 (0.92, 1.30)	NR
Decreased lung function in children			
Six City[B]	*$PM_{15/10}$ (50 μg/m^3)*	*NS Changes*	*20-59*
Six City[C]	*TSP (100 μg/m^3)*	*NS Changes*	*39-114*
24 City[I]	*H^+ (52 nmoles/m^3)*	*-3.45% (-4.87, -2.01) FVC*	*6.2-41.0*
24 City[I]	*$PM_{2.1}$ (15 μg/m^3)*	*-3.21% (-4.98, -1.41) FVC*	*18.1-67.3*
24 City[I]	*SO_4^- (7 μg/m^3)*	*-3.06% (-4.50, -1.60) FVC*	*9.1-17.3*
24 City[I]	*PM_{10} (17 μg/m^3)*	*-2.42% (-4.30, -.0.51) FVC*	*22.0-28.6*
12 Southern California communities[J] (all children)	PM_{10} (25 μg/m^3) acid vapor (1.7 ppb)	-24.9 (-47.2, -2.6) FVC -24.9 (-65.08, 15.28) FVC	28.0-84.9 0.9-3.2 ppb

12 Southern California communities[J] (all children)	PM_{10} (25 $\mu g/m^3$) acid vapor (1.7 ppb)	-32.0 (-58.9, -5.1) MMEF -7.9 (-60.43, 44.63) MMEF	28.0-84.9 0.9-3.2 ppb
12 Southern California communities[K] (4th grade cohort)	PM_{10} (51.5 $\mu g/m^3$) $PM_{2.5}$ (25.9 $\mu g/m^3$) $PM_{10-2.5}$ (25.6 $\mu g/m^3$) acid vapor (4.3 ppb)	-0.58 (-1.14, -0.02) FVC growth -0.47 (-0.94, 0.01) FVC growth -0.57 (-1.20, 0.06) FVC growth -0.57 (-1.06, -0.07) FVC growth	NR
12 Southern California communities[K] (4th grade cohort)	PM_{10} (51.5 $\mu g/m^3$) $PM_{2.5}$ (25.9 $\mu g/m^3$) $PM_{10-2.5}$ (25.6 $\mu g/m^3$) acid vapor (4.3 ppb)	-1.32 (-2.43, -0.20) MMEF growth -1.03 (-1.95, -0.09) MMEF growth -1.37 (-2.57, -0.15) MMEF growth -1.03 (-2.09, 0.05) MMEF growth	NR

Decreased lung function in adults

AHSMOG, So. Calif.[L] (% predicted FEV_1, females)	PM_{10} (cutoff of 54.2 d/yr >100 $\mu g/m^3$)	+0.9 % (-0.8, 2.5) FEV_1	52.7 (21.3, 80.6)
AHSMOG, So. Calif.[L] (% predicted FEV_1, males)	PM_{10} (cutoff of 54.2 d/yr >100 $\mu g/m^3$)	+0.3 % (-2.2, 2.8) FEV_1	54.1 (20.0, 80.6)
AHSMOG, So. Calif.[L] (% predicted FEV_1, males whose parents had asthma, bronchitis, emphysema)	PM_{10} (cutoff of 54.2 d/yr >100 $\mu g/m^3$)	-7.2 % (-11.5, -2.7) FEV_1	54.1 (20.0, 80.6)
AHSMOG, So. Calif.[L] (% predicted FEV_1, females)	SO_4^- (1.6 $\mu g/m^3$)	NS; Not reported	7.4 (2.7, 10.1)
AHSMOG, So. Calif.[L] (% predicted FEV_1, males)	SO_4^- (1.6 $\mu g/m^3$)	-1.5 % (-2.9, -0.1) FEV_1	7.3 (2.0, 10.1)

* Range of mean PM levels given unless, as indicated, studies reported overall study mean (min, max), or mean (±SD); NR=not reported.

[A]Results calculated using PM increment between the high and low levels in cities, or other PM increments given in parentheses; NS Changes = No significant changes.

References:
[B]Dockery et al. (1989)
[C]Ware et al. (1986)
[D]Dockery et al. (1996)
[E]Abbey et al. (1995a,b,c)
[F]Peters et al. (1999a)
[G]McConnell et al. (1999)

[H]Berglund et al. (1999)
[I]Raizenne et al. (1996)
[J]Peters et al. (1999b)
[K]Gauderman et al. (2000)
[L]Abbey et al. (1998)

1 et al., 1998). Associations were also found with sulfates and O_3, but not SO_2, in males. In two-

2 pollutant models, the coefficients for PM_{10} and sulfates were found to remain unchanged or

3 increase in size, while O_3 and SO_2 were reduced and lost statistical significance.

1   Numerous long-term studies of respiratory effects have been conducted in non-North

2   American countries, and many report significant associations between indicators of long-term PM

3   exposure and either decreases in lung function or increased respiratory disease prevalence

4   (summarized in Table 6-23 of the draft CD). These new findings are consistent with those of the

5   previous review as well as with findings of associations between short-term PM exposure and

6   increased respiratory symptoms or decreased lung function. Long-term PM exposures (months to

7   years) may be associated with decreased lung function growth or increased incidence of respiratory

8   disease, but there are still few publications for these effects, and the results are not entirely

9   consistent or conclusive. However, the overall results from the non-North American studies lend

10   general support to the coherence of respiratory effects associated with long-term PM exposure

11   reported across disciplines and health studies.

12   **3.3.3.3   Effects on the Cardiovascular System**

13   In the last review, evidence was available from a number of epidemiology studies indicating

14   that PM was associated with increased mortality and hospital admissions for cardiovascular

15   diseases. These findings inspired further research so that an expanded body of evidence is

16   available in this review from toxicology, epidemiology, and controlled human exposure studies. As

17   described above, new epidemiological evidence generally supports the previous findings. In

18   addition, new evidence from controlled human exposure, toxicological and epidemiological studies

19   indicates that exposure to ambient PM, PM from combustion sources, or PM surrogates may be

20   associated with additional cardiovascular health endpoints such as changes in heart rate variability

21   and plasma fibrinogen levels.

22   PM was first linked with arrhythmia in toxicological studies, notably in an important new

23   series of studies using inhalation exposure to CAPs. Changes in electrocardiogram (ECG)

24   patterns, increased heart rate variability and decreased heart rate have been reported in a

25   toxicology study using dogs exposed to CAPs (Godleski et al., 2000). The CD concludes that the

26   findings for heart rate variability and ECG changes, respectively, suggest both pro- and anti-

27   arrhythmic responses (CD, p. 8-31). The ECG changes included increases in the S-T peak, which

28   suggests that CAPs can augment the ischemia associated with coronary artery blockage in this

29   animal model (CD, p. 8-32).

1   Similarly, altered ECG pattern was reported in ROFA-treated spontaneously hypertensive

2   rats (Kodavanti et al., 2000). However, Muggenberg et al. (2000) reported no consistent changes

3   in ECG pattern in ROFA-treated beagle dogs. Increased arrhythmia was reported in rats exposed

4   to ROFA and to urban particles collected in Ottawa; no cardiac effects were reported with

5   exposure to Mt. St. Helens volcanic ash, which is one form of crustal material (Watkinson et al.,

6   2000). Watkinson and colleagues used several animal models in this study, and reported

7   exaggerated effects in rats that had been treated with monocrotaline, including premature

8   mortality. Some effects were also reported in healthy rats, though mortality only occurred in the

9   compromised animals. Increased mortality was reported in a previous study using ROFA

10   exposures in monocrotaline-treated rats, and the authors also reported serious arrhythmic events in

11   normal rats exposed to ROFA (Watkinson et al., 1998). The draft CD concludes that "animal

12   studies have provided initial evidence that high concentrations of inhaled or instilled particles can

13   have systemic, especially cardiovascular, effects. In the case of [monocrotaline-treated] rats, these

14   effects may be lethal." (CD, p. 8-34).

15   In addition, one new epidemiological study used data on discharge frequency from

16   implanted cardiac defibrillators; discharges occur when the patient is experiencing cardiac

17   arrythmia. Peters et al. (2000) reported generally positive associations between increased

18   defibrillator discharges and PM_{10}, $PM_{2.5}$, and particulate black carbon, but the associations were

19   only significant for $PM_{2.5}$.

20   In several studies, tests of cardiac function (e.g., heart rate, heart rate variability) were

21   done repeatedly for panels of elderly people over a period of several weeks. Generally, increased

22   heart rate and decreased heart rate variability are associated with increased mortality from

23   cardiovascular disease; further discussion of these cardiac health measures is included in Appendix

24   B to Chapter 6 of the draft CD. Most new studies reported decreases in several measures of heart

25   rate variability with increased PM (Liao et al., 1999; Gold et al., 2000; Pope et al., 1999c), though

26   Pope et al. (1999c) reported a significant increase with one measure of short-term heart rate

27   variability for PM_{10}. Significant associations were reported between $PM_{2.5}$ and heart rate

28   variability in panel studies conducted in Baltimore and Boston (Liao et al., 1999; Gold et al.,

29   2000). Gold et al. (2000) did not find associations between heart rate variability and $PM_{10-2.5}$, or

30   with O_3, CO or SO_2.

1   The findings on changes in heart rate are less consistent than those for heart rate variability.

2 In Utah Valley, Pope et al. (1999b) reported a significant increase in heart rate with ambient PM_{10}

3 concentration, but no association with oxygen saturation, using a larger cohort of elderly subjects

4 than in the first study. An association was also reported between TSP and increased heart rate

5 (Peters et al., 1999) in a European study; significant increases were also found with SO_2, though

6 the authors observe that SO_2 may be acting as an indicator for inhalable particles in this study.

7 However, decreased heart rate was reported in the Boston panel study (Gold et al., 2000);

8 associations were also found with NO_2 and SO_2, but the associations with $PM_{2.5}$ were more stable

9 and retained significance in two-pollutant models. Decreased heart rate was also reported in an

10 animal study using intratracheal installation of urban PM (but not with Mt. St. Helens volcanic ash)

11 (Watkinson et al., 2000). In a study using rats and hamsters, no effects were reported in hamsters,

12 but increased heart rate and blood cell differential counts were reported in rats (Gordon et al.,

13 2000).

14   Some studies have reported increases in blood components or characteristics. Fibrinogen is

15 a blood clotting factor and it is released in inflammatory processes; it has been reported to be a risk

16 factor for ischemic heart disease and cerebrovascular disease, and it contributes to blood plasma

17 viscosity (Gardner et al., 2000). In humans exposed to concentrated ambient fine PM, fibrinogen

18 levels were increased in blood obtained 18 hours after exposure, and some inflammatory effects

19 were also reported (Ghio et al., 2000). In a European cohort of heart patients, increased

20 fibrinogen levels were a significant risk factor for the occurrence of cardiovascular events, and

21 there was evidence for an interaction between PM (measured as BS) and fibrinogen levels

22 (Prescott et al., 2000). However, fibrinogen level was not associated with PM exposure in another

23 European epidemiology study (Seaton et al., 1999).

24   Using data from an existing European cohort study, conducted during a time period that

25 included an episode of unusually high pollution levels, associations were reported between TSP

26 and levels of C-reactive protein, which is an indicator of inflammation, tissue damage and infection,

27 and generally related to increased risk of coronary events or ischemic syndromes (Peters, et al.,

28 2000). Associations were also reported with increased plasma viscosity (associated with increased

29 risk of heart attacks) in the blood and levels of TSP, though the associations were not statistically

30 significant (Peters et al., 1997). This study also reported associations with SO_2 and CO that

1   reached statistical significance for women, but not for men. Increased C-reactive protein was

2   reported to be associated with ambient PM_{10} in one epidemiology study in the United Kingdom

3   study (Seaton et al., 1999).

4   A number of toxicology studies have also reported such hemolytic effects as changes in

5   blood factors such as hemoglobin levels or platelet counts. Using animals exposed to CAPs,

6   analyses were done with PM components and factor analysis methods were used to assess effects

7   of PM from different sources. None of the PM factors was associated with changes in platelet

8   count, but several factors or components were associated with changes in counts of inflammatory

9   cells, such as white blood cells (Clarke et al., 2000). The sulfur factor was associated with

10   decreases in red blood cell counts and hemoglobin levels, while some inflammatory changes were

11   reported to be associated with the aluminum/silica factor and the vanadium/nickel factor. In this

12   study, no associations were reported with concentrated fine PM mass. One new epidemiology

13   study does not show significant changes in blood factors such as hemoglobin levels or platelet

14   counts, but does find changes in red blood cell count (Seaton et al., 1999).

15   Though the number of these studies is small, and there are some inconsistencies in findings

16   between studies, these results are generally coherent with findings of increased mortality or

17   hospital admissions for cardiovascular diseases. It should be noted that what appear to be

18   inconsistencies in findings may reflect differing levels of sensitivity and ability to distinguish

19   exposure and temporal features across studies from different disciplines. Regarding the

20   epidemiology studies, the draft CD concludes: "The above findings add support for some

21   intriguing hypotheses regarding possible mechanisms by which PM exposure may be linked with

22   adverse cardiac outcomes. They are especially interesting in terms of implicating both increased

23   blood viscosity and C-reactive protein, a biological marker of inflammatory responses thought to

24   be predictive of increased risk for serious cardiac events" (CD, p. 6-140). Animal toxicology

25   findings were generally consistent with findings of human studies, though as observed previously,

26   there are inconsistencies between studies for a number of individual effects.

27   The results of new epidemiological studies show PM exposure to be associated with excess

28   risk of mortality or hospital admissions for cardiovascular diseases. The results of panel studies,

29   controlled human exposure studies, and animal toxicology studies generally provide coherence

30   with the findings from community health studies in finding associations with increased heart rate,

1   decreased heart rate variability, increases in inflammatory substances such as C-reactive protein,

2   and in plasma viscosity or blood fibrinogen levels. It must be recognized that these findings are

3   from only a few studies and there are a few inconsistencies in findings between studies; caution is

4   also urged when comparing studies conducted in differing animal models and using high dose or

5   exposure levels. Nonetheless, these findings shed some light on potential mechanisms for the

6   associations with increased mortality or hospital admissions for cardiovascular diseases observed in

7   epidemiology studies.

8

9   **3.3.4. Consistency and Coherence of Health Effects Evidence**

10   The 1996 Staff Paper pointed out the inherent limitations in trying to determine the role of

11   PM by examining even the most thorough studies of individual cities that show associations

12   between ambient PM and various health effects. Accordingly, the staff presented a more

13   comprehensive synthesis that considered the consistency and coherence of the available evidence in

14   evaluating the likelihood of PM being causally associated with the observed effects (EPA, 1996b,

15   V-54 to 58). While significantly more evidence of associations between ambient PM and health

16   effects is now available, including multi-city studies that address some of the single-city limitations,

17   it is still important to consider the consistency and coherence of the available evidence as a whole.

18   As discussed in the last review, consistency of an association is evidenced by repeated

19   observations by different investigators, in different places, circumstances and time; and by the

20   consistency of the association with other known facts (EPA, 1996a, Chapter 13; Bates, 1992).

21   Beyond considering the consistency of associations for individual health endpoints, coherence

22   refers to the logical or systematic interrelationship between different health indices that would be

23   expected to be seen across studies of different endpoints or from different disciplines. The

24   consistency and coherence of the expanded body of evidence now available is discussed and

25   evaluated below.

26   **3.3.4.1 Consistency**

27   The 1996 Criteria Document summarized over 80 community epidemiological studies

28   evaluating associations between short-term PM levels and mortality and morbidity endpoints in a

29   number of locations throughout the world, using a variety of statistical techniques, of which over

30   60 studies found consistent, positive, significant associations (EPA, 1996a, Tables 12-2 and 12-8

1   to 12-13). The 1996 Staff Paper displayed the relative risk estimates for mortality and morbidity

2   effects associated with PM_{10} from the U.S. and Canadian studies, concluding that despite the

3   variations in study locations and approaches, the estimates for each health endpoint were relatively

4   consistent among the studies; although, as would be expected, some variation was seen (EPA,

5   1996b, B-55 and Figure V-2).

6   As discussed above, since the last review, more than 70 new PM-mortality studies alone

7   have been published, as well as a large number of new morbidity studies, and several major multi-

8   city studies. The draft CD notes that the effects estimates from the new studies in the U.S. and

9   throughout the world are generally consistent with those observed in the last review, not only from

10 PM_{10} multi- and single-city studies (shown above in Figures 3-4 and 3-7 from U.S. and Canadian

11 studies for mortality and hospital/ER admissions, respectively), but also from the significantly

12 expanded body of studies of fine-fraction (e.g., $PM_{2.5}$) particles (similarly shown above in Figures

13 3-5 and 3-8) (CD, p. 6-266). The evidence from coarse-fraction ($PM_{10-2.5}$) studies (as shown

14 above in Figures 3-6 and 3-9), while somewhat expanded, remains more limited and presents more

15 difficulty in attempting to draw conclusions about the consistency of the reported associations

16 across studies (CD, p. 6-267). Bringing together the findings for $PM_{2.5}$ from all U.S. and Canadian

17 studies for a range of health endpoints from mortality to varying indices of morbidity, Figure 3-10

18 shows that the effects estimates for each health endpoint are relatively consistent among the

19 studies, very similar to the consistent pattern observed for PM_{10} studies in the last review (EPA,

20 1996b, Figure V-2).

21   Looking more closely at the variations for particular endpoints observed across cities

22 within the 90-city NMMAPS study reveals more heterogeneity of city-specific PM_{10}-mortality

23 effects estimates than in the past review (as discussed above in Section 3.3.1.1.1). At least some

24 of the increased variability is to be expected based on a study design that includes areas with more

25 limited PM sampling days and population sizes than is usual for single-city publications. The CD

26 presents some evidence that the inter-city variability may, at least in part, simply reflect imprecise

27 PM effect estimates derived from smaller-sized analyses (of less extensive available air pollution

28 data or numbers of deaths) tending to obscure more precise estimates from larger-size analyses for
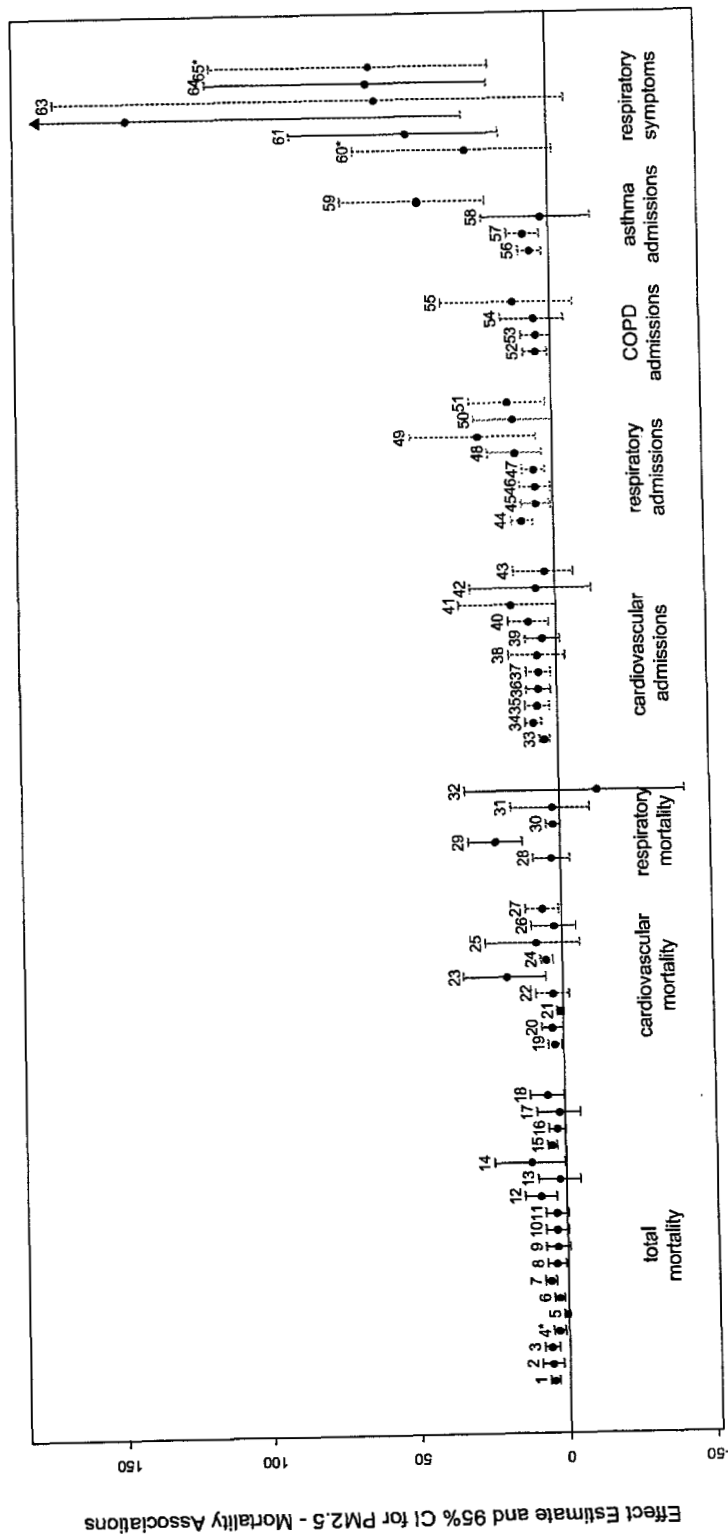
Effect Estimate and 95% CI for PM2.5 - Mortality Associations

Figure 3-10. Estimated excess mortality and morbidity risks per 25 μg/m³ PM₂.₅ from U.S. and Canadian studies (listed below), showing consistency and coherence across the different effects categories. Within each category, results are ranked by decreasing natural log of the mortality- or morbidity-days product. Multi-city studies denoted with an asterisk.

Total Mortality:
1. Burnett et al., 1998, Toronto. Canada
2. Schwartz, 2000c Boston, MA
3. Goldberg et al., 2000, Montreal, Canada
4. Burnett et al., 2000, 8 Canadian cities
5. Ostro et al., 1995, So. California
6. Schwartz et al., 1996, St. Louis. MO
7. Schwartz et al., 1996, Boston, MA
8. Schwartz et al., 1996, Knoxville, TN
9. Schwartz et al., 1996, Portage, WI
10. Lippmann et al, 2000, Detroit, MI
11. Mar et al., 2000, Phoenix, AZ
12. Fairley, 1999, Santa Clara, CA
13. Schwartz et al., 1996, Topeka, KS
14. Ostro et al., 2000, Coachella Valley, CA

15. Tsai et al., 2000, Newark, NJ
16. Schwartz et al., 1996, Steubenville, OH
17. Tsai et al., 2000, Elizabeth, NJ
18. Tsai et al., 2000, Camden, NJ
Cardiovascular Mortality:
19. Moolgavkar et al., 2000, Los Angeles, CA
20. Goldberg et al, 2000, Montreal, Canada
21. Ostro et al., 1995 So. California
22. Lippmann et al, 2000, Detroit, MI
23. Mar et al, 2000, Phoenix, AZ
24. Tsai et al, 2000, Newark, NJ
25. Ostro et al., 2000, Coachella Valley, CA
26. Tsai et al., 2000, Elizabeth, NJ
27. Tsai et al., 2000, Camden, NJ

Respiratory Mortality:
28. Moolgavkar. 2000a, Los Angeles
29. Goldberg et al., 2000, Montreal, Canada
30. Ostro et al., 1995, So. California
31. Lippmann et al., 2000. Detroit, MI
32. Ostro et al., 2000, Coachella Valley, CA
Cardiovascular Admissions:
33. Moolgavkar, 2000b, Los Angeles, CA
34. Burnett et al., 1999, Toronto, Canada (IHD)
35. Burnett et al., 1999, Toronto, Canada (HF)
36. Burnett et al., 1999, Toronto, Canada (dysrhythmia)
37. Burnett et al., 1999, Toronto, Canada
38. Tolbert et al., 2000, Atlanta, GA)
39. Lippmann et al., 2000, Detroit, MI (IHD)
40. Lippmann et al., 2000, Detroit, MI (HF)
41. Stieb et al, 2000, St. John, Canada
42. Tolbert et al., 2000a, Atlanta, GA (dysrhythmia)
43. Lippmann et al, 2000, Detroit (dysrhythmia.)

Respiratory Admissions:
44. Burnett et al., 1999, Toronto, Canada (resp. infection)
45. Lumley and Heagerty, 1999, Seattle, WA (PM1)
46. Stieb et al., 2000, St. John, Canada
47. Burnett et al., 1999, Toronto, Canada
48. Lippmann et al., 2000, Detroit, MI (pneumonia)
49. Delfino et al., 1997, Montreal, Canada
50. Delfino et al, 1998, Montreal, Canada
51. Thurston et al, 1994, Toronto, Canada
COPD Admissions:
52. Moolgavkar, 2000c, Los Angeles, CA
53. Burnett et al, 1999, Toronto, Canada
54. Lippmann et al., 2000, Detroit, MI
55. Tolbert et al., 2000a, Atlanta, GA

Asthma Admissions:
56. Burnett et al., 1999, Toronto. Canada
57. Sheppard et al., 1999, Seattle, WA
58. Tolbert et al., 2000, Atlanta, GA
59. Norris et al., 1999, Seattle, WA
Respiratory Symptoms:
60. Schwartz and Neas, 1999, 6 U.S. city reanalysis (cough)
61. Neas et al., 1996, State College, PA (cough)
62. Neas et al., 1995, Uniontown, PA (cough)
63. Neas et al., 1996, State College, PA (wheeze)
64. Neas et al, 1996, State College, PA (cold)
65. Schwartz and Neas, 1999, 6 U.S. city reanalysis (lower resp. symptoms)

1   other locations, which tend to be consistently more positive and statistically significant (CD, p. and

2   6-260 to 6-263). The variability may also be due to other analytical factors, or reflect an as yet

3   unexplained location-specific difference in exposures or weather and air pollution mixes (CD, p 6-

4   260). The CD also discusses the suggestion of regional heterogeneity in the quantitative estimates,

5   which suggest larger effects estimates for the Northeast Southern California than other regions (CD

6   p 6-263, 6-264). It is as yet unclear whether these are significant and real differences, or whether

7   related to analytical or city/sampling size issues. The CD notes that, if real, such differences would

8   not be inconsistent with potential regional differences in particle size/composition or population

9   exposure patterns (CD, p6--264). While warranting further study, the observed inter-city and

10   regional variations in the NMMAPS do not call into question the qualitative consistency observed

11   across all the available studies, including the combined results from the available multi-city studies.

12   In further considering the consistency of the reported PM effects, it is important to evaluate

13   the sensitivity of the PM estimates to the differing levels of co-pollutants present in various study

14   locations. Such an evaluation supplements the multi-city and single city analyses discussed in earlier

15   sections. In the last review, this analysis examined PM_{10} effects estimates, to consider whether the

16   reported PM effects can be interpreted appropriately as being likely independent effects attributable

17   to PM, or whether the evidence suggests that the reported PM effects likely result from the

18   influence of other pollutants present in the ambient air in the study locations, either through

19   confounding or effects modification. As discussed in the 1996 Staff Paper, if PM is acting

20   independently, then a consistent association should be observed in a variety of locations of differing

21   levels of co-pollutants. On the other hand, if the reported PM effects are confounded or modified

22   by any of the co-pollutants, then the reported PM effects would be expected to show a trend of

23   being higher in areas with relatively high concentrations of the confounding co-pollutant and lower

24   in areas with relatively low co-pollutant concentrations (EPA, 1996b, V-55). Figure 3-11 shows

25   the reported $PM_{2.5}$ mortality effects estimates (from single-pollutant models) from U.S. and

26   Canadian studies relative to the levels of O_3, NO_2, SO_2, and CO present in the study locations. As

27   was seen in the last review for PM_{10} (EPA, 1996b, Figure V-3a,b), the magnitude and statistical

28   significance of the associations reported between $PM_{2.5}$ and mortality in these studies
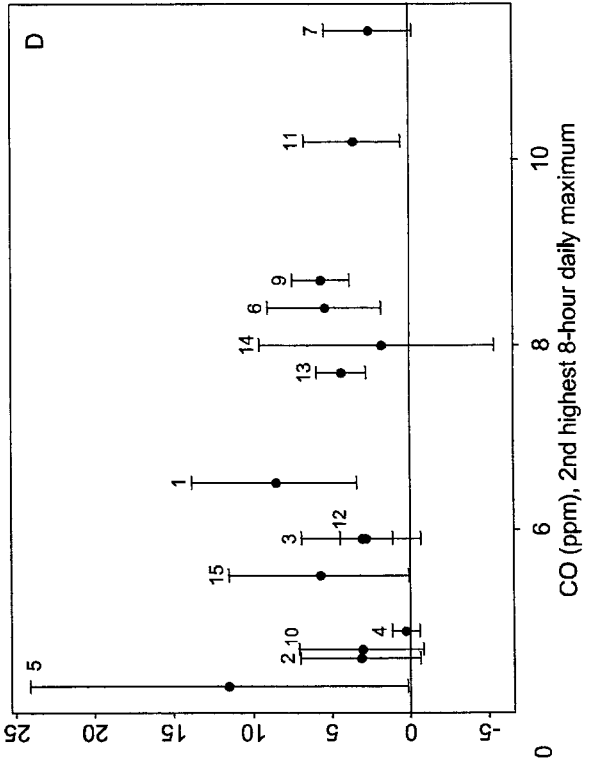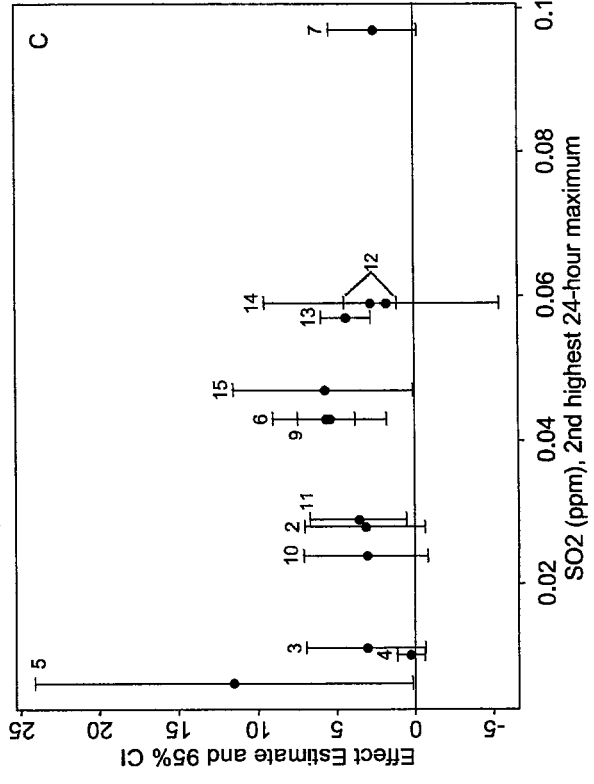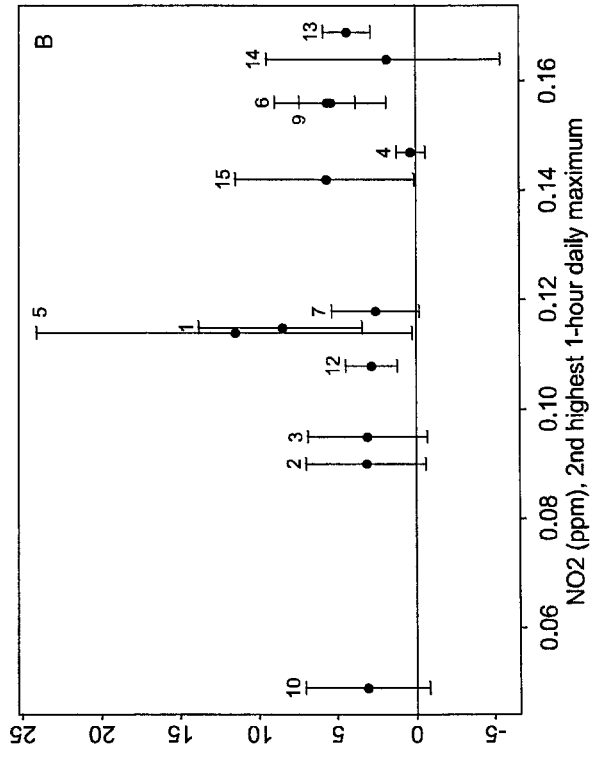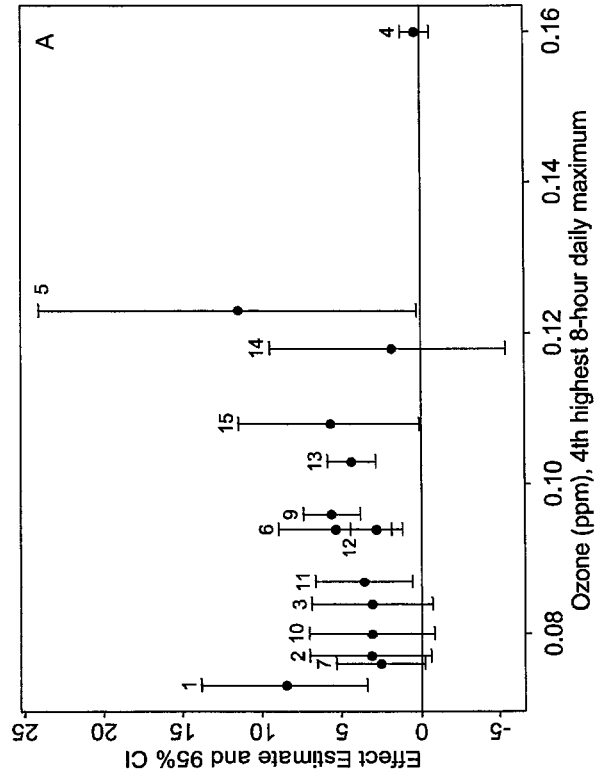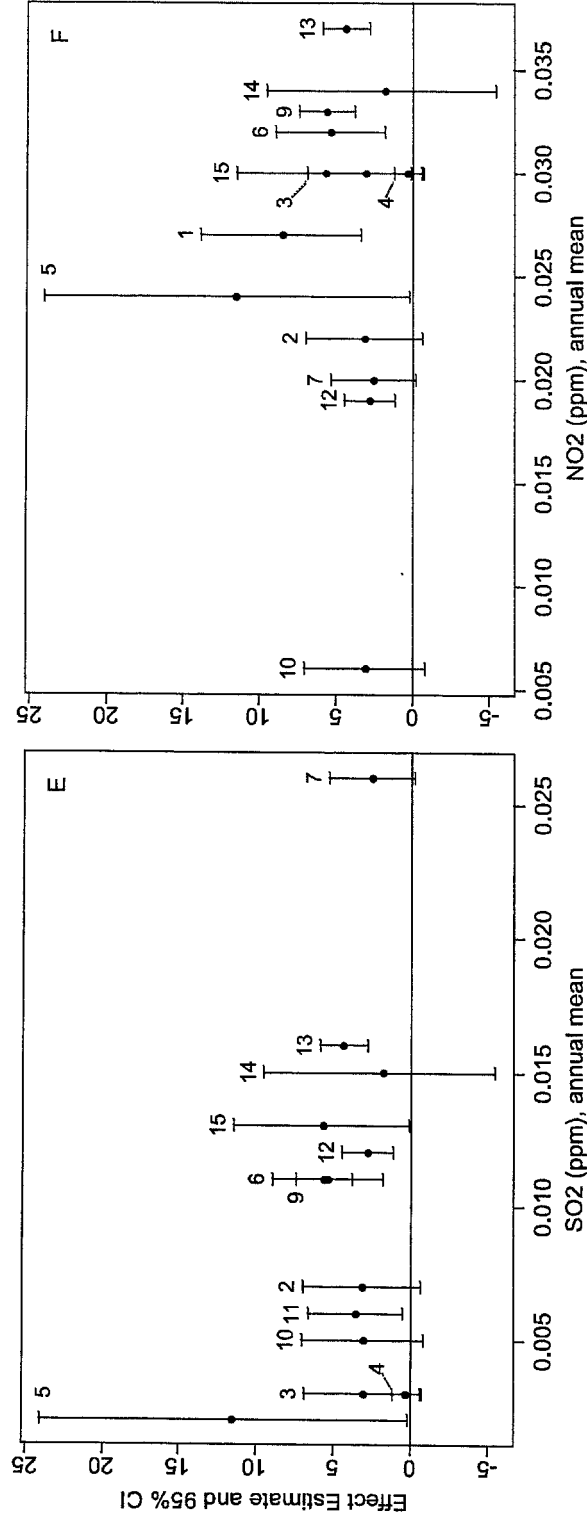
Figure 3-11. Associations between $PM_{2.5}$ and total mortality from U.S. studies, plotted against gaseous pollutant concentrations from the same locations. Air quality data obtained from the Aerometric Information Retrieval System (AIRS) for each study time period: (A) mean of 4th highest 8-hour ozone concentration; (B) mean of 2nd highest 8-hour CO concentration; (C) mean of 2nd highest 1-hour NO_2 concentration; (D) mean of 2nd highest 24-hour SO_2 concentration; (E) annual mean SO_2 concentration; (F) annual mean NO_2 concentration. Study locations are identified below (data in Appendix 3-A, Table 5)

1. Fairley, 1999, Santa Clara
2. Lippmann et al., 2000, Detroit
3. Mar et al., 2000, Phoenix
4. Ostro et al., 1995, So. California
5. Ostro et al., 2000, Coachella Valley

6. Schwartz 2000c, Boston
7. Schwartz et al., 1996, Boston
8. Schwartz et al., 1996, Knoxville
9. Schwartz t al., 1996, Portage
10. Schwartz et al., 1996, St. Louis

11. Schwartz et al., 1996, Steubenville
12. Schwartz et al., 1996, Topeka
13. Tsai et al., 2000, Camden NJ
14. Tsai et al., 2000, Elizabeth NJ
15. Tsai et al., 2000, Newark NJ

1 show no trends with the levels of any of the four gaseous co-pollutants. While not definitive, these

2 consistent patterns indicate that it is more likely that there is an independent effect of $PM_{2.5}$, as well

3 as PM_{10}, that is not confounded or appreciably modified by the gaseous pollutants.

4   More specific information relevant to evaluation of potential confounding or effects

5 modification for each of the four major gaseous co-pollutants is discussed below in Section 3.5.1.

6 **3.3.4.2 Coherence**

7   In addition to the consistently observed associations for each of these effects, the newly

8 available epidemiological and toxicological evidence reinforces and adds to the coherence in the

9 kinds of health effects associated with PM exposure noted in the last review (EPA, 1996b, V-56).

10 The 1996 Criteria Document provided a qualitative review of the coherence of the health effects

11 associated with both short- and long-term exposure to PM (EPA, 1996a, Tables 13-6 and 13-7). In

12 that review, it was noted that PM is related to a number of logically linked effects of both the

13 respiratory and cardiovascular systems. Respiratory system effects included premature mortality

14 and increased hospital and emergency room admissions for respiratory-related causes, as well as

15 increased respiratory disease and symptoms and decreased lung function. Cardiovascular system

16 effects included premature mortality and increased hospital and emergency room admissions for

17 cardiovascular-related causes. In addition to this observed qualitative coherence, quantitative

18 coherence was also observed in that the increases in respiratory- and cardiovascular-related hospital

19 admissions were more frequently occurring than the increases in mortality for the same causes,

20 based on reported relative risk estimates and baseline population incidence statistics (EPA, 1996a,

21 Table 13-8).

22   The newly available evidence of PM-related effects expands upon the previously observed

23 qualitative coherence. New PM-related effects associations have now been reported, including

24 increased physicians' visits for respiratory causes and various new cardiovascular-related endpoints,

25 that serve to fill in the spectrum of observed effects from physiological changes that are linked to

26 more serious health outcomes through premature mortality. The new epidemiologic and

27 toxicologic evidence on cardiovascular-related endpoints discussed in Section 3.3.3.3 above is

28 suggestive of coherence in effects on the cardiovascular system for ambient measured as CAPs,

29 $PM_{2.5}$, or PM_{10}. It is important to note the draft CD cautions that the findings should be viewed

1 as providing limited or preliminary support for PM-related cardiovascular effects (CD, p. 6-268).

2 Changes in heart rate or heart rate variability are linked with more serious cardiovascular outcomes,

3 including increased risk of heart attacks. The findings of increased levels of fibrinogen or plasma

4 viscosity indicate a potential link between ambient PM exposure and the occurrence of ischemic

5 events, and the increases seen in blood factors such as C-reactive protein provide evidence for

6 inflammatory changes that can be linked with more serious cardiac effects.

7 The new evidence also continues to support the quantitative coherence observed in the last

8 review. For example, in the NMMAPS studies, 2.6% and 3.5% increases in total and

9 cardiorespiratory mortality, respectively, were reported for a 50 $\mu g/m^3$ increase in daily PM_{10}, while

10 increases in hospital admissions of 6% (for cardiovascular causes, with a range across other studies

11 of approximately 3% to 10%) and 10% (for COPD or pneumonia, with a range across other studies

12 of approximately 5% to 25% for respiratory-related causes) were similarly reported. In addition,

13 several new studies have reported associations with visits to physicians' offices for respiratory

14 disease, ranging from 3% to 42% increases for a 50 $\mu g/m^3$ increase in daily PM_{10}. In the new

15 studies on lung function changes or respiratory symptoms incidence, increases in risk of respiratory-

16 related symptoms range up to over 50% per 50 $\mu g/m^3$ increase in daily PM_{10}. Updated baseline

17 incidence rates for respiratory and heart diseases reported in the draft CD (p. 9-102 to 9-103),

18 considered together with these illustrative ranges of effects estimates (and with the ranges shown

19 above in Figures 3-3 through 3-10), continue to show that the quantitative coherence across all

20 PM-related endpoints, especially for PM_{10} as well as for $PM_{2.5}$, is consistent with expectations (CD,

21 p. 6-267 to 6-268). Further, as noted in the last review (EPA, 1996b, V-57), the larger effects

22 estimates reported in long-term exposure studies are coherent with the smaller effects estimates

23 reported for associations with daily changes in PM concentrations. As noted above in the

24 discussion of consistency, the limited amount of information available on $PM_{10-2.5}$ presents more

25 difficulty in attempting to draw conclusions about coherence of effects of coarse-fraction particles.

26 As noted in the last review, the coherence of PM-related effects is further strengthened by

27 studies demonstrating associations with a range of effects in the same population, as illustrated by

28 studies in a number of locations (EPA, 1996b, V-57). For example, studies in Utah Valley have

29 shown a number of closely related health outcomes associated with PM exposures, including

30 decreased lung function, increased respiratory symptoms, increased medication use in asthmatics,

1 and increased elementary school absences (frequently due to upper respiratory illness) (EPA,

2 1996b, V-57).

3   In summary, these observations suggest coherence from subtle changes in lung function or

4 heart rate variability to increased mortality from cardiorespiratory diseases reported in

5 epidemiological studies. Taken as a whole, the newly available health studies together with studies

6 available in past reviews show general coherence for PM-related effects in the respiratory and

7 cardiovascular systems. The expanded evidence for coherence in effects, along with previously

8 described observations of marked consistency in the results of recent studies and those available in

9 the last review, support a causal link between PM, especially as indexed by PM_{10} and $PM_{2.5}$, and

10 effects on the cardiovascular and respiratory systems (CD, p. 6-266 to 6-267).

11

12 **3.4   SENSITIVE GROUPS FOR PM-RELATED HEALTH EFFECTS**

13   In general, subpopulations that have been identified in previous PM NAAQS reviews as

14 being potentially more sensitive to the adverse health effects of PM have included individuals with

15 respiratory and cardiovascular disease, the elderly, children, and asthmatic individuals (EPA 1996b,

16 pp. V-33 to V-36). As summarized in the draft CD, Section 9.7, new studies continue to support

17 consideration of these subpopulations as potentially sensitive to PM.

18   ***Individuals with respiratory and cardiovascular disease:*** Numerous epidemiology studies

19 have identified individuals with cardiorespiratory diseases (e.g., asthma, COPD) as being at greater

20 risk for adverse effects with PM exposure (CD, p. 9-99). Most notably, one recent epidemiology

21 study (Goldberg et al., 2000) linked mortality data with information on preexisting health conditions

22 (e.g., pharmaceutical prescriptions, medical visits) to investigate differences between groups

23 according to health status. The authors reported that associations between $PM_{2.5}$, COH or sulfates

24 and total mortality were increased among individuals with preexisting acute lower respiratory

25 disease, congestive heart failure, and any cardiovascular disease. New information from studies of

26 cardiovascular health measures such as plasma viscosity or changes in heart rate or heart rate

27 variability provides additional support for consideration of persons with cardiovascular disease as

28 being susceptible to the PM-related effects (CD, p. 9-112).

29   Asthma has been of particular public interest as a respiratory condition that may lead to

30 sensitivity to air pollution effects. Included in Appendix A, Table 2, are numerous epidemiology

1   studies reporting increased medical visits for asthma with exposure to PM_{10}, $PM_{2.5}$ or $PM_{10-2.5}$, and

2   most studies reported significant associations. In considering asthmatics as a susceptible

3   subpopulation, the results for studies evaluating changes in lung function and respiratory symptoms

4   were evaluated separately for asthmatic and nonasthmatic subjects. The draft CD reported that

5   asthmatic subjects had greater reduction in pulmonary function with PM exposure, but both

6   asthmatic and non-asthmatic subjects had similar responses in respiratory symptom studies (CD

7   Section 6.3.3.1). A number of toxicology studies have evaluated the effects of particles or

8   surrogate particles on allergic diseases, including allergic asthma, and the draft CD finds that

9   "[t]hese studies provide biological plausibility for the exacerbation of allergic asthma associated

10 with episodic exposure to PM" (CD, p. 8-45).

11   New dosimetry studies have shown that, among people with COPD, airflow may be

12 unevenly distributed due to airway obstruction, resulting in deeper penetration of particles in the

13 better ventilated regions, or increased local deposition of particles. In addition, ventilation rate and

14 rate of air flow is often increased with airway obstruction. The findings of these studies suggest

15 that total lung deposition generally is increased with obstructed airways, regardless of deposition

16 distribution between the tracheobronchial or alveolar regions (CD, p. 7-22).

17   A number of animal models of susceptible populations have been used in toxicology studies

18 examining PM. These include: monocrotaline treatment of rats as a model of cardiorespiratory

19 disease; SO_2-induced chronic bronchitis in rats; ovalbumin sensitization in rodents as a model of

20 airway hyperresponsiveness; and genetically predisposed animals such as the spontaneously

21 hypertensive rat. The advantages and disadvantages of these animal models are discussed more

22 fully in Section 8.4 of the draft CD. While recognizing that further research is needed, the draft CD

23 concludes that these studies "have consistently shown that animals with compromised health, either

24 genetic or induced, are more susceptible to instilled or inhaled particles, although the increased

25 animal-to-animal variability in these models has caused problems" (CD, p. 8-87).

26   *Age-related subpopulations:* In the previous review, numerous studies indicated that the

27 elderly and children are more susceptible to PM-related health effects (EPA, 1996a, p. 12-364).

28 Similarly, in reviewing the recent studies of PM-related medical visits or admissions/visits for

29 respiratory diseases, the draft CD finds that the groups identified as being most strongly affected by

30 PM are older adults and the very young (CD, p. 6-172). Goldberg et al. (2000) also report that

1   associations between PM and mortality were generally larger among persons greater than 65 years

2   of age, which is consistent with the findings of numerous previous studies. Several new

3   epidemiology studies have reported significant associations between PM exposure and intrauterine

4   growth reduction or low birth weight, known to be infant health risk factors, as well as excess infant

5   mortality (CD, p. 9-106).

6   In addition, the draft CD highlights findings of a number of new studies that raise the

7   possibility that deposition may be greater in children than adults; it is also noted that children's

8   generally higher activity levels with accompanying higher ventilation rates might contribute to

9   increased particle deposition (CD, p. 7-20). However, dosimetric evidence has not identified

10   elderly adults to be at increased risk due to difference in lung deposition, clearance or retention of

11   inhaled particles associated with aging, per se, though the draft CD concludes that "[p]robably of

12   much more importance in placing elderly adults at increased risk for PM effects is the higher

13   propensity for such individuals to have preexisting cardiovascular or respiratory disease conditions."

14   (CD, p. 9-106).

15   *Other Subpopulations:* Other subpopulations have been evaluated as potentially

16   susceptible groups in recent studies. New dosimetry studies have indicated that total lung

17   deposition and deposition peaks may be greater in females than in males (CD Section 7.2.3.1), and

18   one new epidemiology study reported that associations between PM_{10} and mortality were greater in

19   females than males (Zanobetti and Schwartz, 2000). However, the reverse was found in the

20   AHSMOG prospective cohort (described in Section 3.3.1.2) and no gender differences were

21   reported in the largest prospective cohort studies (Six Cities and ACS).

22   Zanobetti and Schwartz (2000) did not find differences in PM_{10}-mortality associations in

23   analyses stratified by race or education level (an indicator of socioeconomic status). Yet with long-

24   term PM exposure, Krewski et al. (2000) reported greater mortality effects among those with lower

25   levels of education. There is as yet insufficient evidence to identify new subpopulations as being

26   potentially susceptible to PM-related effects. In summary, the findings of new epidemiology,

27   dosimetry and toxicology studies provide support for previous findings that individuals with

28   respiratory and cardiovascular disease, individuals with infections, the elderly, children, and

29   asthmatic individuals are subpopulations that may be more sensitive to the adverse health effects of

30   ambient PM exposure.

1 ## 3.5   EVALUATION OF PM-RELATED HEALTH EFFECTS EVIDENCE

2   In the preceding sections, evidence from new health studies has been summarized and

3 integrated with findings from previous reviews. As has been seen in previous reviews, much of the

4 health evidence is taken from epidemiology studies, though critical new insights are offered in the

5 results of toxicology and controlled human exposure studies. The 1996 CD and Staff Paper

6 discussed, at some length, issues related to the interpretation and evaluation of epidemiological

7 evidence. While recognizing that additional research was needed on some issues, the 1996 CD

8 concluded that "the epidemiologic findings cannot be wholly attributed to inappropriate or incorrect

9 statistical methods, misspecification of concentration-effect models, biases in study design or

10 implementation, measurement errors in health endpoint, pollution exposure, weather, or other

11 variables, nor confounding of PM effects with effects of other factors" (EPA, 1996a, p. 13-92). In

12 this section, the new findings relevant to the interpretation of epidemiological information will be

13 discussed.

14   In the evaluation of the health effects evidence, one important consideration is the evidence

15 for health effects of PM alone or in the presence of co-pollutants. Throughout the preceding

16 discussions on the nature of health effects associated with PM, and the consistency and coherence

17 of the health evidence, consideration of potential confounding by co-pollutants has been discussed.

18 Here, additional considerations relevant to each of the four major gaseous co-pollutants will be

19 discussed in Section 3.5.1.

20   In addition, new information is available on potential health effects of PM components or

21 source-related PM, as summarized in Section 3.5.2. Several additional key issues are discussed in

22 the draft CD, and the new information that would inform this NAAQS review is summarized in

23 Section 3.5.3 for: (1) the lag period between exposure and occurrence of health effects; (2) the

24 exposure time window for effects, specifically relating acute exposure periods of hours to days with

25 health effects; (3) the influence of model specification on epidemiology findings; and (4) the

26 influence of exposure error or exposure misclassification on reported PM-health associations.

27

28 ### 3.5.1 Additional Evidence on the Role of Gaseous Co-pollutants

29   In the preceding sections, several methods for assessing potential confounding by co-

30 pollutants were discussed (i.e., multi-pollutant modeling in multiple or single locations, assessing

1   the relationship between PM-mortality associations and the PM-co-pollutant correlation, and

2   observing the relationships between PM-health effect estimates and co-pollutant concentrations).

3   The results of these analyses generally support an independent association between PM and health

4   effects such as mortality or hospital admissions or emergency room visits for cardiorespiratory

5   diseases. In this section, additional information is summarized for each of the major gaseous co-

6   pollutants identified as potential confounding factors or effects modifiers for PM-health

7   associations.

8   *Ozone.* As observed in the 1996 Staff Paper, among the gaseous co-pollutants, there is

9   greater potential for O_3 to be a confounder in studies of respiratory effects (EPA, 1996b, p. V-51).

10   Ozone has been found to have independent effects on the respiratory system; for example, increased

11   hospital admissions and emergency room visits for respiratory causes have been associated with

12   ambient O_3 exposures (EPA 1998, p. 25). Among recent studies, the PM effect estimates for

13   COPD (but not pneumonia) hospital admissions were reduced in Lippmann et al. (2000), and

14   Tolbert et al. (2000a) and Delfino et al. (1998) reported reductions in effects estimates for PM_{10} and

15    $PM_{2.5}$ with asthma admissions when O_3 was included in the model. However, associations between

16   PM indices and hospital admissions for respiratory disease remained significant in models containing

17   O_3 in Toronto (Burnett et al., 1997), and in a number of the European and Latin American studies

18   highlighted in Table 6-17 of the draft CD.

19   The epidemiology studies showed little evidence of confounding by O_3 for associations

20   between PM and cardiovascular mortality or morbidity. In the multi-city epidemiology studies,

21   associations between mortality and PM (including $PM_{2.5}$ or $PM_{10-2.5}$, where available) were relatively

22   unaffected by the addition of O_3 to the models (10 U.S. cities, Schwartz et al., 2000; 8 Canadian

23   cities, Burnett et al., 2000). The draft CD concludes that PM and O_3 can be most clearly separated

24   as having independent effects, compared with other gaseous co-pollutants. (CD, p. 9-81).

25   Co-pollutants can serve not only as confounders or effect modifiers, but there may be

26   interactive effects reported with co-exposure to multiple pollutants. Recent animal toxicology

27   studies have tested effects of exposure to PM or PM surrogates (e.g., urban PM, carbon particles,

28   acid aerosols) in combination with O_3 (CD, Table 8-10). In two Canadian studies, co-exposure to

29   O_3 and urban particles potentiated the effects reported with O_3 alone (Bouthillier et al., 1998;

1 Vincent et al., 1997), while mixed results were reported from studies using combinations of acid

2 aerosols and O_3 (CD Table 8-10).

3 ***Carbon monoxide.*** CO reduces oxygen delivery to the body's organs and tissues, and the

4 health threat from CO is most serious for those who suffer from cardiovascular disease, such as

5 angina pectoris (EPA, 1998, p. 10). Thus, CO may be expected to potentially confound

6 associations between PM and cardiovascular mortality or morbidity. It is considered less likely that

7 CO would confound associations with respiratory effects.

8 New studies have generally reported associations between PM and mortality (especially

9 from total or respiratory causes) to be unaffected when CO was added to two-pollutant models

10 (Lippmann et al., 2000; Burnett et al., 1998). Little evidence of confounding was also reported in

11 two-pollutant models for respiratory admissions/visits. However, in some studies of

12 admissions/visits for cardiovascular diseases, the PM effects sizes were reduced in two-pollutant

13 models with CO. Reflecting also the evidence summarized in the recent CD for CO, the draft CD

14 finds that "[a]mong the gaseous criteria pollutants, CO has emerged as the most consistently

15 associated with cardiovascular (CVD) hospitalizations. The CO effects are generally robust in the

16 multi-pollutant model, sometimes as much so as PM effects. However, the typically low levels of

17 ambient CO concentrations in most such studies and minimal expected impacts on

18 carboxyhemoglobin levels and consequent associated hypoxic effects thought to underlie CO CVD

19 effects complicate interpretation of the CO findings and argue for the possibility that CO may be

20 serving as a general surrogate for combustion products (e.g., PM) in the ambient pollution mix."

21 (CD, p. 9-73).

22 As observed in the 1996 Staff Paper, exposure misclassification may introduce significant

23 problems in interpreting epidemiological findings on CO-related effects, due to the nature of urban

24 and indoor sources of CO (EPA, 1996b, p. V-52). While CO has been reported to cause cardiac

25 effects in the higher concentrations used in controlled human exposure studies, it is unlikely that CO

26 is confounding the effects associated with ambient PM in the more recent epidemiological studies.

27 ***Sulfur dioxide.*** Potential confounding between PM and SO_2 has been evaluated in some

28 detail in previous reviews. As stated in the 1996 Staff Paper, both PM (measured as TSP or black

29 smoke) and SO_2 were elevated during the historical pollution episodes such as those occurring in

30 London during the 1950's, and the concentrations of SO_2 and PM were highly correlated due to

1   common emissions sources. A number of epidemiological analyses evaluated potential confounding

2   for PM and SO_2 in associations with mortality, and in some studies it was difficult to distinguish

3   effects of SO_2 and PM. It was observed, however, that SO_2 generally does not penetrate into the

4   deeper portions of the lung, based on evidence from dosimetry and controlled human exposure

5   studies. In addition, SO_2 concentrations are generally low indoors (where people spend the greatest

6   part of their time) due to rapid removal by indoor surfaces. Staff concluded that "it is unlikely that

7   SO_2 is responsible for all or the observed associations between PM and mortality" (EPA, 1996b, p.

8   V-49).

9   Newly published epidemiological studies generally find no evidence of confounding in

10 associations with mortality or hospital admissions or emergency room visits with short-term PM

11 exposures when SO_2 is included in models. However, in the reanalysis of long-term studies

12 (discussed in Section 3.3.1.2), significant associations were reported between mortality and sulfur

13 dioxide, and in multiple pollutant models the sulfur dioxide associations often appeared stronger

14 than those for fine particles and sulfates. However, the SO_2 associations were also reduced in two-

15 pollutant models, and the correlation between SO_2 and sulfates makes it difficult to distinguish their

16 effects. In the results of toxicology studies with co-exposure to PM and SO_2, there was little

17 evidence for interaction with particles in causing effects (CD Table 8-10).

18   *Nitrogen dioxide.* NO_2 exposure has been associated with changes in airway responsiveness

19 and pulmonary function in individuals with preexisting respiratory illnesses and increases in

20 respiratory illnesses in children (Trends report, p. 20). In multi-pollutant models available from the

21 new epidemiology studies, inclusion of NO_2 in the models has varying effects on the effect estimate

22 for PM_{10}. Lippmann et al. (2000), for example, reports results for total, cardiovascular, and

23 respiratory mortality, as well as hospital admissions for a number of specific respiratory or

24 cardiovascular diseases. In two-pollutant models with NO_2, the PM effects are often relatively

25 unaffected, but when substantial changes are noted, the PM effect may be either increased or

26 decreased. Moolgavkar (2000b) finds that NO_2 reduces effect estimates between PM_{10} and

27 cardiovascular admissions in Cook County, IL, but not in Los Angeles County, CA or Maricopa

28 County, AZ. The 1996 Staff Paper recognized that, especially in the western U.S., NO_x emissions

29 can be a major source of fine particles, which makes it difficult to distinguish effects of the two

30 pollutants (EPA, 1996b, p. V-53).

1   *Summary.* The CD concludes "Overall, it appears, however, that ambient PM and O_3 can

2   be most clearly separated out as likely having independent effects, their concentrations often not

3   being highly correlated. More difficulty is encountered, at times, in sorting out whether NO_2, CO,

4   or SO_2 are exerting independent effects in cities where they tend to be highly correlated with

5   ambient PM concentrations, possibly because of derivation of important PM constituents from the

6   same source (e.g., NO_2, CO, PM from mobile sources) or a gaseous pollutant (e.g., SO_2) serving as

7   a precursor for a significant PM component (e.g., sulfate)" (CD, p. 9-81).

8   In interpreting the findings of these multi-pollutant analyses, it is important to recognize that

9   there are issues in co-pollutant confounding that multi-pollutant models may not be able to address.

10   Inclusion of pollutants that are highly correlated with one another can lead to misleading

11   conclusions in identifying a specific causal pollutant. For example, collinearity between pollutants

12   may occur if the gaseous pollutants and PM come from the same sources, or if PM constituents are

13   derived from gaseous pollutants (e.g., sulfates from SO_2) (CD, p. 6-227). Sources of PM

14   constituents include combustion of various fuels, gasoline or diesel engine exhaust, and some

15   industrial processes (CD, Table 9-2); these sources also emit gaseous pollutants. When collinearity

16   exists, multi-pollutant models would be expected to produce unstable and statistically insignificant

17   effect estimates for both PM and the co-pollutants (CD, p. 9-81).

18   Some investigators have raised the possibility that PM may be a key surrogate or marker for

19   a larger subset of pollutants in the overall ambient air pollution mix (CD, p. 9-39). Given the

20   heterogeneous nature of PM, co-pollutants may also be indicators for fine particles derived from

21   specific combustion sources. For example, when CO is included in a two pollutant model with

22    $PM_{2.5}$, CO may serve as an indicator for that portion of total $PM_{2.5}$ that is derived from mobile

23   source emissions.

24   It is also important to consider differences in population exposures to the ambient

25   pollutants. The link between ambient PM concentrations, measured at centrally-located monitors,

26   and individuals' exposures to ambient PM is discussed at length in Chapter 5 of the CD and

27   Sections 2.8 and 3.5.3.3 of the Staff Paper. In considering exposure to the gaseous pollutants as

28   well, the CD states, "it is also significant to note that, although ambient concentrations of a number

29   of gaseous pollutants (O_3, NO_2, SO_2) often are found to be highly correlated with various PM

30   parameters, personal exposures to these gases are not correlated highly with personal exposure to

1   PM indicators. The correlations of the ambient concentrations of these gases also are not

2   correlated highly with the personal exposure to these gases. Therefore, when significant statistical

3   associations are found between these gases and health effects, it could be that these gases may, at

4   times, be serving as surrogates for PM rather than being causal themselves. Pertinent information

5   on CO has not been reported." (CD, p. 9-85)

6   Taking into consideration the findings of single- and multi-city studies and other evaluations

7   of potential confounding by gaseous co-pollutants described in preceding sections, the evidence

8   generally indicates that PM, alone or in combination with other pollutants, has independent effects

9   on morbidity and mortality. In reviewing the epidemiological evidence, the draft CD concludes that

10   "[o]verall, although such issues may warrant further evaluation, it appears unlikely at this time that

11   such confounding accounts for the vast array of effects attributed to ambient PM . . ." (CD, p. 9-

12   81).

13

14   **3.5.2 PM Components or Sources**

15   Much of the focus of the preceding discussions on the nature of PM-related effects has been

16   epidemiological studies that use gravimetric PM measurements, with an emphasis on PM_{10}, $PM_{2.5}$

17   and $PM_{10-2.5}$. However, there is a growing body of information on effects associated with PM

18   components, smaller ultrafine particles, or PM associated with specific sources. In the 1996 CD,

19   evidence from toxicological studies on the effects of acid aerosols, metals, ultrafine particles, diesel

20   emission particles, silica, and bioaerosols was available. Among the recent studies are epidemiology

21   analyses on the effects of ultrafine particles or studies using factor analysis to evaluate the effects of

22   PM from different sources. The following sections will discuss, to the extent that information is

23   available, evidence on health associations with ultrafine particles and other PM components or

24   source-related PM.

25

1   **3.5.2.1 Ultrafine Particles**

2   As described in Chapter 2, ultrafine particles generally include particles smaller than 0.1 μm

3   in diameter and are considered nuclei-mode particles. Ultrafine particles are a portion of fine PM;

4   they predominate in the number of particles, but comprise only a small portion of fine PM mass.   It

5   has been suggested, based on toxicological evidence, that ultrafine particles may be more toxic than

6   larger particles. It has also been proposed that particle surfaces, or the chemical composition of

7   particle surfaces, may be responsible for PM toxicity, and ultrafine particles have relatively large

8   surface areas (CD, p. 8-68).

9   The toxicology studies available to date addressing potential effects of ultrafine particles

10   have used PM surrogates or model particles, such as ultrafine carbon or TiO_2 particles. Several

11   new studies are reviewed in the draft CD with somewhat mixed findings on whether greater effects

12   are reported with ultrafine particles than with fine particles. However, in studies using metal oxide

13   dusts, the health response was increased with increasing total surface area, suggesting that particle

14   surface chemistry is an important component of biological responses (CD, p. 8-71). Overall, the

15   draft CD concludes that there is insufficient toxicological evidence to conclude that ambient

16   ultrafine particle concentrations are more strongly linked to health effects than mass concentrations

17   of fine particles (CD, p. 8-85).

18   A limited number of epidemiological studies, all conducted in European nations, have

19   evaluated health associations with ultrafine particles. One study reported associations between total

20   mortality and both fine particle mass and ultrafine particle number count data, with effects of about

21   the same magnitude reported for each PM size fraction. The authors concluded that both fine and

22   ultrafine particles showed independent effects on mortality at ambient concentrations (Wichmann et

23   al., 2000). Three studies, using panels of asthmatic children or adults, have reported associations

24   between ultrafine particles and increased symptoms or decreased pulmonary function. All reported

25   associations with both ultrafine particle number concentrations and mass concentrations of BS,

26   $PM_{2.5}$ or PM_{10}. In one study, the authors concluded that health effects associations were greater

27   with fine than with ultrafine particles, though significant associations were reported with both

28   (Peters et al., 1997). The authors of the other two studies concluded that separating the effects of

29   different particle size classes was difficult (Pekkanen et al., 1997; Tiittanen et al., 1999), and

1   Pekkanen et al. (1997) concluded that stronger associations were found with BS or PM_{10} mass than
2   with ultrafine particle counts.
3   Finally, some new evidence from human exposure studies has indicated that infiltration rates
4   for ultrafine particles into buildings are lower than those for fine (accumulation mode) particles
5   (CD, p. 9-24). This would suggest that community exposure to PM is greater for fine particles than
6   ambient ultrafine particles, and makes it unlikely that health associations found with ambient $PM_{2.5}$
7   are truly reflecting underlying associations with ultrafine PM. The results of recent epidemiological
8   and toxicological investigations indicate that health effects may be associated with ultrafine particle
9   number or total particle surface area, but the overall findings do not indicate that exposure to
10   ultrafine particles results in greater health responses than PM mass concentrations.

11   **3.5.2.2 Other PM Components, PM Sources**
12   As briefly discussed above, a number of toxicology studies on effects of PM components or
13   surrogates were available during the previous review. In addition, a substantial body of
14   epidemiological studies had evaluated relationships between mortality and morbidity and ambient
15   sulfate or acid aerosol concentrations. The 1996 CD concluded that the epidemiology studies
16   suggest that strongly acidic PM, including sulfates as an indicator of acid aerosols, was associated
17   with both acute and chronic health effects (EPA, 1996a, p. 12-253).
18   Recent studies have evaluated the effects of not only numerous PM components (e.g.,
19   sulfates, nitrates, acids, metals, elemental carbon, biological components), but also PM from
20   different sources (e.g., motor vehicle or industrial emissions, crustal material). Among
21   epidemiological studies that examined the effects of specific components of PM, most commonly
22   used were sulfates and acids, COH, and elemental carbon or organic carbon (as indicators of motor
23   vehicle emissions). Some evidence is reported for associations with components or PM source
24   indicators in community health studies, as outlined below. A larger body of evidence on effects of
25   specific PM components is available from toxicological studies. Regarding the animal toxicology
26   study results, the draft CD concludes that "[t]o date, toxicology studies on PM have provided only
27   very limited evidence for specific PM components being responsible for observed cardiorespiratory
28   effects of ambient PM" (CD, p. 8-83).
29   As was reported in the previous review, numerous epidemiology studies have indicated that
30   both mortality and morbidity effects are associated with ambient exposures to sulfates and acid

1   aerosols (H$^+$). Similarly, associations reported in recent studies between ambient sulfates and

2   mortality are positive and most are statistically significant (CD, figure 6-5). The draft CD

3   concludes that, in these studies, the relative significance of sulfate and H$^+$ varied from city to city,

4   and the associations were stronger in cities where the sulfate and H$^+$ levels were relatively high (CD,

5   p. 6-66). Significant associations were reported using sulfates as the PM indicator in the studies of

6   long-term PM exposure and mortality (CD, Tables 6-14 and 6-15). A number of respiratory

7   medical visit studies included assessment of associations with sulfates or acids and also reported

8   significant associations (CD, pp. 6-166 to 6-168).

9   One new study with exposures to CAPs in dogs reported an association between the sulfur

10   factor of the particles with changes in red blood cell count and hemoglobin levels (Clarke et al.,

11   2000). However, considering the remaining literature from toxicological and controlled human

12   exposure studies using exposure to acid aerosols (CD, Table 8-1), the draft CD concludes that the

13   new studies are consistent with the findings from the previous review, where it was concluded that

14   effects were reported in toxicological or controlled human exposure studies only when levels were

15   very high, although "acid components should not be ruled out as possible mediators of PM health

16   effects" (CD, p. 9-100). One difference between the epidemiological and toxicological studies is

17   that the epidemiological studies were measuring sulfates or acidity of the ambient aerosol, while

18   toxicological studies were using exposures to acid aerosols alone. The draft CD concludes that

19   interactions between different metals and the acidity of PM were reported to influence the severity

20   and kinetics of lung injury induced by ROFA and its soluble transition metals (CD, p. 8-21). This

21   suggests that interaction between some PM components may be an important factor in some health

22   effects associations.

23   Elemental carbon and organic carbon concentrations were used in studies conducted in

24   Atlanta (Klemm and Mason, 2000) and Phoenix (Mar et al., 2000). Both were significant

25   predictors of mortality in the Phoenix study, but no PM indicators were reported to be significantly

26   associated with mortality in the Atlanta study, possibly due to its small sample size. The draft CD

27   observes that the correlation between COH, elemental carbon and organic carbon and other mobile

28   source related pollutants (fine PM, NO$_2$, CO) were high, and concludes that the results reported in

29   these analyses suggest that "PM components from mobile sources are likely associated with

30   mortality" (CD, p. 6-65).

1   The 1996 CD concluded that effects of bioaerosols (e.g., endotoxin) were reported in

2 toxicological or controlled human exposure studies only when levels were very high. The recent

3 toxicological and controlled human exposure studies on the effects of ambient bioaerosols, primarily

4 endotoxins, are summarized in draft CD Table 8-6. These studies of workers exposed in

5 agricultural settings showed respiratory changes, such as reduced lung function or increased airway

6 responsiveness, with increasing dust or endotoxin exposure levels. These occupational study

7 findings were supported by evidence for inflammatory responses in animal or controlled human

8 exposure studies. However, the endotoxin levels measured in these studies were far greater than

9 levels generally reported in ambient air. The draft CD concludes "although these exposures are

10 massive compared to endotoxin levels in ambient PM in U.S. cities, these studies serve to illustrate

11 the effects of endotoxin and associated bioaerosol material in healthy nonsensitized individuals"

12 (CD, p. 8-25). In addition, a number of epidemiology studies have associations of mold spore

13 concentrations on lung function or asthma symptom severity (Delfino et al., 1996, 1997; Neas et al.,

14 1996). In evaluating the results of new epidemiology studies on the association between mortality

15 and coarse fraction particles, the draft CD suggests that the findings of associations in some areas

16 "hint at possible contributions of biogenic materials (e.g., molds, endotoxins, etc.) to the observed

17 coarse particle effects" but sufficient evidence is not yet available to support or refute this

18 hypothesis (CD, p. 9-57).

19   From toxicological studies, the most substantive new evidence is provided for effects of

20 metals and diesel exhaust particles. For diesel exhaust particles, the draft CD finds growing

21 evidence from toxicology studies that diesel PM exacerbates the allergic response to inhaled

22 antigens, and indications that the organic constituents of diesel PM may contribute to these effects.[7]

23

24   Metals, especially water soluble metals, have been reported to cause cell injury and

25 inflammatory changes in toxicology studies, but it is not clear that these effects are found with the

26 small metal concentrations reported in ambient PM (CD, p. 8-85). The transition metals, such as

27 iron, vanadium or nickel, have been most commonly associated with adverse effects in toxicology

28 studies. As summarized by Costa and Dreher (1997), a number of toxicology studies have shown

---

[7] Evidence from both epidemiological and toxicological studies is evaluated in detail in the draft Diesel Health Assessment Document (EPA, 2000b).

1   that effects were more closely linked to the metal content of particles than particle mass, though

2   some studies have not found strong associations with particulate metals (e.g., Soukup et al., 2000).

3   Limited evidence is available from epidemiology studies, though one new study reported

4   associations between mortality and particulate iron, nickel and zinc in 8 Canadian Cities (Burnett et

5   al., 2000).

6   Four new epidemiological studies and one toxicological study have used factor analysis to

7   investigate health associations with PM ($PM_{2.5}$ and PM_{10} or PM_{15}) from different sources (Laden et

8   al., 2000; Mar et al., 2000; Tsai et al., 2000; Ozkaynak et al., 1996; Clarke et al., 2000). These

9   studies used elements or other PM components as indicators of the emissions sources; for example,

10   Laden et al. (2000) use silicon as an indicator for fine particles of crustal or geologic origin (CD,

11   Table 6-5). In addition to testing associations between PM mass and mortality, the four studies

12   evaluated relationships with the PM source factors. The four epidemiology studies are fairly

13   consistent in finding associations for mortality with indicators of PM (both $PM_{10/15}$ and $PM_{2.5}$) from

14   combustion sources, but not from geologic sources (CD, pp. 6-67 to 6-72). The draft CD

15   concludes that the results of the epidemiology studies generally indicate that a "number of

16   combustion-related source-types were associated with mortality, including motor vehicle emissions,

17   coal combustion, oil burning and vegetative burning" (CD, p. 6-78).

18   In the toxicological study, dogs were exposed to CAPs and numerous indicators of lung

19   injury or inflammation (e.g., white blood cell counts, protein in lung lavage fluid) and cardiovascular

20   health (e.g., platelet and red blood cell counts, hemoglobin or fibrinogen levels) were measured

21   (Clarke et al., 2000). While little evidence was reported for effects with fine PM mass, the authors

22   also conducted factor analysis and identified four PM factors: aluminum/silicon, sulfur,

23   vanadium/nickel, and bromine/lead. The sulfur factor was linked with decreases in red blood cell

24   counts and hemoglobin levels, while the aluminum/silicon and vanadium/nickel factors were linked

25   with inflammatory changes, such as increases in neutrophils or white blood cell counts. The authors

26   conclude that specific components of particles may be responsible for effects, but do not distinguish

27   PM sources that would be linked to each of the PM factors or components.

28   The effects of PM of crustal or geologic origin were also investigated in two

29   epidemiological studies that used meteorological data in conjunction with air quality data to identify

30   days where wind-blown crustal particles predominate. Both studies reported no evidence of

1   associations between mortality and wind-blown crustal particles (Schwartz et al., 1999; Pope et al.,

2   1999). In contrast, another study, conducted in Coachella Valley, CA, where coarse particles of

3   geologic origin predominate PM_{10} concentrations, reported significant associations between

4   mortality and PM_{10} (Ostro et al., 1999). Taken together, the draft CD finds that the results of these

5   studies suggest that particles of crustal origin (whether in the fine or coarse fraction of PM) are not

6   likely associated with acute mortality (CD, pp. 6-56 to 6-58). However, the draft CD observes that

7   "crustal" particles may carry biological components (e.g., endotoxin), pesticides or herbicides (as

8   may occur in agricultural situations), or components of emissions from vehicles, smelters, or other

9   industrial operations (CD, p. 6-274). In addition, the existing studies have assessed only mortality

10   as a health endpoint, and there are numerous morbidity indices of potential concern.

11   These recent studies provide some new evidence for health effects associations with many

12   different PM components such as sulfates, acids and metals. For mortality, the factor analysis

13   studies appear to implicate ambient PM from combustion-related sources in associations with total

14   mortality, but not particles of crustal or geologic origin (CD, p. 9-61). Recognizing that ambient

15   PM exposure has been associated with increases in numerous health indices, the evidence is still too

16   limited to allow identification of which PM components or sources might be more toxic than others,

17   and growing evidence indicates that there are numerous potentially toxic PM components and there

18   may also be interaction occurring between components.

19

20   **3.5.3 Issues Regarding Interpretation of Epidemiology Studies**

21   The 1996 CD included extensive discussions of methodological issues for epidemiological

22   studies, including questions about model specification or selection, and measurement error in

23   pollutant measurements and exposure error. As summarized in the 1996 Staff Paper, PM-health

24   effects associations reported in epidemiological studies were not likely an artifact of model

25   specification, since analyses or reanalyses of data using different modeling strategies reported

26   similar results (EPA 1996b, p. V-39). In the 1996 CD, less information was available to

27   quantitatively evaluate the potential influence of measurement or exposure error in interpreting

28   epidemiological study findings. A few new publications have explored these questions, and the

29   findings are summarized here. Finally, little information was available for the 1996 CD to allow

1 comparison of differing lag periods or exposure time windows for PM-related health effects; the

2 recent studies have provided some new information, as discussed below.

3 **3.5.3.1 Lag Periods**

4   Many epidemiological studies on the health effects of acute PM exposure have tested

5 several lag periods, or time delays between the pollution measurement and the occurrence of the

6 health outcome being measured. Commonly used lags are 0 day (effects occurring on the same day

7 as the pollution measurement), 1 to several days, or average pollution measures over several days

8 preceding the health outcome. Often, several lag periods are tested, and the results for the most

9 statistically significant lag period are reported in the publication. As stated in the draft CD, "While

10 this practice may bias the chance of finding a significant association, without a firm biological

11 reason to establish a fixed pre-determined lag, it appears reasonable" (CD, p. 6-238). An

12 alternative approach, the distributed lag, has been introduced in several new studies; the effect of

13 pollution on health is assessed as the effect of a weighted average pollution variable, recognizing

14 that effects of air pollution can occur on several subsequent days.

15   In the NMMAPS analysis of PM_{10} associations with total mortality, lag periods of 0, 1 and 2

16 days were used across all cities. The authors reported associations with all three lags, with the

17 largest association being reported for a 1-day lag period. As stated in the draft CD, "since the

18 cardiovascular, respiratory or other causes of acute mortality usually associated with PM are not at

19 all specific, there is little *a priori* reason to believe that they must have the same relation to current

20 or previous PM exposures at different sites" (CD, p. 6-239). In fact, the most significant lag period

21 varied somewhat between NMMAPS study locations, though the range is only from 0-day to 2-day

22 lag periods (draft CD Table 6-24). Several new studies have shown that lag periods may vary for

23 different causes of death; for example, Rossi et al (1999) reported stronger associations between

24 deaths from respiratory infections or heart failure with same-day TSP concentrations, and between

25 myocardial infarction and COPD with TSP lagged 3-4 days (CD, p. 6-232).

26   For morbidity effects, the findings are similar. The draft CD reports that time series studies

27 of hospital admissions or emergency room visits for cardiovascular diseases suggest that the

28 strongest effects are reported at lag 0, with some effects seen at lag 1 but little beyond a one-day

29 lag (CD, p. 6-137). But in evaluating admissions for specific disease categories, Lippmann et al.

30 (2000) reported the most significant associations between PM_{10} lagged 0 days and pneumonia,

1   while the "best" lags for heart failure, ischemic heart disease and COPD were 1 day, 2 days and 3

2   days, respectively. Burnett et al. (2000) also reported significant associations between PM_{10} and

3   dysrhythmia with a 0-day lag, with asthma and heart failure for an average of PM_{10} concentrations

4   over the 0-2 day lags, and with obstructive lung disease at a 2-day lag. In the NMMAPS evaluation

5   of PM_{10} associations with hospital admissions among the elderly, the distributed lag approach was

6   reported to generally result in stronger associations.

7   In summary, the draft CD states "It may be possible that different PM components may

8   produce effects which appear at different lags or that different preexisting conditions may lead to

9   different delays between exposure and effect. Thus, although maximum effect sizes for PM effects

10 have often been reported for 0-1 day lags, evidence is also beginning to suggest that more

11 consideration should be given to lags of several days . . . higher overall risks may exist than implied

12 by [the] maximum estimated for any particular single or two-day lags." (CD, p. 6-233).

13 **3.5.3.2 Model Specification**

14   The influence of choices made in statistical model specification on the results of

15 epidemiological analyses was examined extensively during the previous NAAQS review. The 1996

16 CD evaluated the effect of different modeling strategies, and the methods used to adjust for

17 meteorological variables, seasonal or long-term trends, and co-pollutants on the results of

18 epidemiological studies (adjustment for co-pollutants was addressed above in Section 3.5.1). The

19 1996 CD reported that health associations reported with PM were relatively insensitive to different

20 methods of weather adjustment, and concluded that the results across studies "are not model

21 specific, nor are they artifactually derived due to misspecification of any specific model. The

22 robustness of the results of different modeling strategies and approaches increases our confidence in

23 their validity" (EPA 1996a, p. 13-54).

24   Among the new studies reviewed in the draft CD are some that use case-crossover methods.

25 The case-crossover study design has only recently been applied in studies of the health effects of air

26 pollutants. This type of study uses the health event (e.g., hospital admission for heart disease) as

27 the case period, and selects a control period from some specific time before or after the event, and

28 assesses whether there are differences in risk factors (air pollutants and other factors) between the

29 periods. The draft CD in Section 6.4.8 presents the findings of three such studies, and all three

1　studies report associations between PM and mortality that are consistent with the results of the

2　more numerous time-series analyses.

3　　　Along with the review of new case-crossover studies, the draft CD also reviews the new

4　evidence on model specification from time-series studies. While identifying some remaining issues

5　needing further study, the draft CD concludes that "[t]hese analyses suggest that the overall findings

6　are not very sensitive to these analytical choices . . ." (CD, p. 6-249).

7　　　The draft CD reviews some new studies that evaluate adjustment for factors other than

8　weather or co-pollutants that have been suggested as potential confounders for PM-related effects.

9　One analysis using a subset of NMMAPS data for 5 cities investigated the influence of respiratory

10　epidemics as a potential confounder for PM_{10}-mortality associations. As summarized in the draft

11　CD (p. 6-44), control for respiratory epidemics only reduced the association between PM_{10} and

12　mortality slightly, from 4.3% to 4.0% with a 50 $\mu g/m^3$ increase in PM_{10}, and the association

13　remained statistically significant (Braga et al., 2000). Schwartz (2000b) evaluated PM_{10}-mortality

14　associations among different socio-economic strata (e.g., race, gender, education level, percent

15　nonwhite) and for deaths in-hospital and outside the hospital. The addition of socioeconomic

16　variables to the models did not modify the PM_{10}-mortality effect estimates, but the effect estimate

17　for deaths occurring outside the hospital was substantially greater than the effect estimate for in-

18　hospital deaths. Pollen count was also examined as a potential confounder for respiratory medical

19　visits, and it was reported that pollen levels did not influence the results (CD, p. 6-181).

20　　　Methods used in assessing effects associated with long-term exposure to pollutants were

21　also reviewed as a part of the reanalysis of the long-term mortality studies (Krewski et al., 2000).

22　The authors applied an array of different models and variables to determine whether the original

23　results would remain robust to different analytic assumptions and model specifications. The draft

24　CD concludes "None of these alternative models produced results that materially altered the original

25　findings" (CD, p. 6-83).

26　**3.5.3.3 Measurement Error**

27　　　In this and previous reviews of the PM NAAQS, much of the health evidence for PM-

28　related effects comes from epidemiological studies where ambient PM measurements are used to

29　represent community PM exposures. One key issue is the use of PM concentrations measured at

30　central locations to represent the community's exposure to ambient PM. As discussed in Section

1   2.8 above, daily changes in individuals' personal exposure to ambient PM is well correlated with

2   daily changes in ambient PM measured as central monitors. Thus, the draft CD concludes that

3   ambient PM concentrations are a useful surrogate for exposure to ambient PM (CD, p. 9-86).

4   Another key issue in interpreting epidemiology study findings is related to error in the

5   measurements of the pollutants. Analyses available for the 1996 Staff Paper indicated that random

6   measurement error in pollutant concentration data is not likely to bias the findings of epidemiologic

7   analyses using these data. However, a remaining question was the existence of differential

8   measurement error, where one pollutant was measured with more error than another, and the effect

9   this might have in comparing epidemiologic findings for the two pollutants (EPA, 1996b, p. V-42).

10   The draft CD summarizes the findings of several new analyses that show the potential

11   influence of differential measurement error on epidemiological analysis results, though the

12   conditions required for the error to substantially influence the epidemiological findings are severe

13   and unlikely to exist in current studies. In simulation analyses of a "causal" pollutant and a

14   "confounder" with differing degrees of measurement error and collinearity between the pollutants it

15   was found that, in some circumstances, a causal variable measured with error may be overlooked

16   and its significance transferred to a surrogate. However, for "transfer of apparent causality" from

17   the causal pollutant to the confounder to occur, there must be high levels of both measurement

18   error in the causal variable and collinearity between the two variables (Zidak et al., 1996; Zeger et

19   al., 1999; Fung and Krewski, 1999). An additional analysis applied measurement error models to

20   data from the Harvard Six Cities study, specifically testing relationships between mortality and

21   either fine or coarse fraction particles. The authors identified several variables that could influence

22   bias in effects estimates for fine- or coarse-fraction particles: the true correlation of fine- and

23   coarse-fraction particles, measurement errors for both, and the underlying true ratio of the toxicity

24   of fine- and coarse-fraction particles. The existence of measurement error and collinearity between

25   pollutants could result in underestimation of the effects of the less well-measured pollutant.

26   However, the authors conclude "it is inadequate to state that differences in measurement error

27   among fine and coarse particles will lead to false negative findings for coarse particles. If the

28   underlying true ratio of the fine and coarse particle toxicities is large (i.e., greater than 3:1), fine

29   particle exposure must be measured significantly more precisely in order not to *underestimate* the

30   ratio of fine particle toxicity versus coarse particle toxicity" (Carrothers and Evans, 2000, p. 72).

1 Thus, while the potential remains for differential error in pollutant measurements to influence the

2 results of epidemiological studies, it is unlikely that the levels of measurement error and correlation

3 between pollutants reported in existing studies would result in transfer of apparent causality from

4 one pollutant to another.

5 The influence of exposure misclassification on the results of epidemiological analyses has

6 been further investigated in one major new analysis that was conducted as a part of NMMAPS

7 (Zeger et al., 2000). Using data collected in previous exposure studies, the authors developed a

8 relationship between personal exposure to ambient particles and ambient PM_{10} concentrations. The

9 authors reported that the association between PM_{10} and mortality using ambient PM_{10}

10 concentrations underestimated the association between personal ambient PM_{10} exposure and

11 mortality.

12 In reviewing these new studies, along with analyses that were available in previous reviews,

13 the draft CD concludes "the studies that examined joint effects of correlation and error suggest that

14 PM effects are likely underestimated, and the spurious PM effects (i.e., qualitative bias such as

15 change in the sign of the coefficient) due to transferring of effects from other covariates require

16 extreme conditions and are, therefore, unlikely." (CD, p. 6-245)

17 **3.5.3.4 Exposure Time Periods for Acute Effects**

18 In the previous PM NAAQS review, epidemiological studies on acute effects of PM

19 exposure primarily used 24-hour average PM concentrations. The newly available epidemiological

20 studies include several where 1-hour or 8-hour average ambient PM concentrations are used in

21 time-series analyses, and some evidence is from panel studies of cardiac patients with average PM

22 concentrations of one to several hours. Toxicology or controlled human exposure studies often use

23 shorter exposure time periods, and a new body of evidence is available from studies using inhalation

24 exposures to ambient particles, including one study of controlled human exposures to CAPs.

25 As discussed earlier, one controlled human exposure study included exposure to

26 concentrated ambient $PM_{2.5}$ for 2 hours, and reported mild increases in neutrophils in

27 bronchoalveolar lavage samples and increased blood fibrinogen levels after the exposure period

28 (Ghio et al., 2000) . Animal toxicology studies have used inhalation exposures to CAPs or PM

29 surrogates with exposure time periods generally in the range of 1 to 6 hours per day, sometimes for

30 several days (CD, Tables 8-3 and 8-7). A range of effects have been reported in these animal

1   studies, including evidence for respiratory effects such as lung injury and inflammation and

2   cardiovascular effects such as arrhythmia. Based on the findings of these studies, it is apparent that

3   acute exposure to PM of a few hours' duration can result in physiological or cellular changes.

4   Several recent epidemiology studies have reported findings for PM averaged over 24 hours

5   and shorter time periods (1-hour and 8-hour) that do not show substantial differences in effects

6   reported for different averaging times. These studies have used data from continuous PM monitors,

7   such as the TEOM or nephelometer (see Chapter 2 for details on monitoring methods), and

8   evaluated associations with total mortality, hospital admissions, heart rate variability and respiratory

9   symptoms. Some studies have reported larger effect estimates for one- or several-hour

10   concentrations than for 24-hour average concentrations, e.g.,1-hour and 8-hour PM_{10} with

11   respiratory symptoms in California (Delfino et al., 1998) and heart rate variability changes with 4-

12   hour $PM_{2.5}$ levels in Boston (Gold et al., 2000). In contrast, larger effect estimate sizes were

13   reported for associations between total mortality and 24-hour $PM_{2.5}$ levels than 1-hour levels in

14   Melbourne and Brisbane, Australia (Simpson et al., 1997, 2000). In two other Australian studies,

15   similar effects were reported for 1-hour and 24-hour $PM_{2.5}$ levels with total mortality in Melbourne

16   (Morgan et al., 1998) and hospital admissions for respiratory disease in Sydney (Morgan et al.,

17   1997).

18   Thus, the results of the recent epidemiology studies time do not provide substantive

19   evidence that mortality or morbidity are more strongly associated with one short-term exposure

20   interval than another. The results of controlled human exposure and animal toxicology provide

21   some evidence that health effects can be result from PM exposures of a few hours' duration; in fact,

22   it is logical to expect that some health effects would be nearly instantaneous while others might

23   require a longer duration of exposure.

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